IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

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AVENTIS PHARMACEUTICALS INC. and SANOFI-AVENTIS US LLC,	:	Civil Action
Plaintiffs,	:	
v.	:	
BARR LABORATORIES, INC.,	:	
Defendant.	:	No. 06-286-GMS

- - -

Wilmington, Delaware
Wednesday, May 21, 2008
9:00 a.m.
Day 3

- - -

BEFORE: HONORABLE GREGORY M. SLEET, Chief Judge

APPEARANCES:

JOHN G. DAY, ESQ.
Ashby & Geddes
-and-
PAUL H. BERGHOFF, ESQ.,
JOSHUA R. RICH, ESQ.,
JEREMY E. NOE, ESQ.,
ANDREW WILLIAMS, ESQ., and
ALLISON BALDWIN, ESQ.
McDonnell Boehnen Hulbert & Berghoff LLP
(Chicago, Illinois)

Counsel for Plaintiffs

APPEARANCES CONTINUED:

KAREN L. PASCALE, ESQ.
Young Conaway Stargatt & Taylor, LLP
-and-
JAMES HURST, ESQ.,
MAUREEN L. RURKA, ESQ.,
TARAS GRACEY, ESQ.,
RENEE SOTOS, ESQ., and
JULIA JOHNSON, ESQ.
Winston & Strawn LLP
(Chicago, Illinois)

Counsel for Defendant

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THE COURT: Good morning. Please be seated. I think the witness can resume the stand.

MR. HURST: Your Honor, two quick issues.

THE COURT: Go ahead.

MR. HURST: One is, we are hopeful and almost expected, our side, to get done a little earlier than the time allotted.

THE COURT: I figured that might happen.

MR. HURST: We wondered if there would be opportunity, I don't know what Your Honor's practices are, for short closing statements.

THE COURT: I really don't think I am going to entertain closing statements in this case. I don't think it is necessary.

MR. HURST: Thank you, Your Honor.

Second quick issue. This morning Aventis hands to me a new exhibit that is not in the pretrial order. I just wanted to make two objections to it.

THE COURT: Is it coming up with this witness?

MR. HURST: It's not.

THE COURT: Okay. Let's hold it.

MR. RICH: Your Honor, if I can make a quick scheduling point.

THE COURT: We are going to break at 11:00. I have a plea. Leave your stuff there. We will have a criminal defendant who will likely be incarcerated. So I will ask you to vacate counsel table.

MR. RICH: One of our witnesses, Dr. Kaliner, is required to be back in his office to provide medical care to patients tomorrow.

We have scheduled him early in the day. But if for some reason the presentation of evidence goes a little longer, and he is still on the stand at 5:00, would it be possible to go a little longer to make sure his testimony gets in?

THE COURT: Oh, yes.

We need to try to do something about the heat again.

... BARRY SIEGEL, previously sworn as a

witness, was examined and testified further as follows ...

DIRECT EXAMINATION CONTINUED

BY MS. RURKA:

Q. Just to refresh the Court's recollection, yesterday we were discussing Dr. Berridge's statistical analysis of the 1998 PET data. Do you recall that?

A. I do.

Q. Will you please pull up Demonstrative 38.

I think you goes mentioned there needs to be a correction applied to the P value to get the correct P value cutoff for these types of data, the Bonferoni correction. Is that right?

A. That's correct.

Q. If you applied that correction, what would the correct P value cutoff be?

A. With the table of data he did the comparisons on, the correct P value, instead of being 0.055, would have been about 0.0002.

Q. So if the numbers were above that number, would that show statistically significant differences?

A. Above that number would not be statistically significant.

Q. If you use that correct P value of .0002, your data, your correct analysis or correct numbers would show statistically significant differences?

A. **They would not.**
Q. **How about Dr. Berridge's numbers?**
A. **Many fewer of the numbers which I believe to be incorrect would now be statistically significant.**
Q. **Statistically significant?**
A. **Dr. Berridge said that many of the values, comparing many of the comparisons of Flonase and Nasacort AQ were highly significant, with the corrected P value many fewer of them would be statistically significant. Most of them would not be significant.**
Q. **Did you reads Dr. Berridge's rebuttal report in this case?**
A. **I did.**
Q. **Do you recall him saying in that report that he had analyzed some videos that he prepared on the 2002 study, analyzing Flonase and Nasacort AQ?**
A. **I do.**
Q. **What were those videos?**
A. **These were movies that showed the motion over the course of time of the radioactive tracer in the nasal cavity, and they are designed to depict, with a broad brush, where the tracer goes, initially, then where it moves to over time.**
Q. **In Dr. Berridge's rebuttal, I think he says that the videos appear to show some qualitative* differences between**

Flonase and Nasacort AQ. Do you agree with him?

A. **Yes, that's what he says. I agree, to the casual observer, if you just look at those images you might perceive that this looks a little different than that. But the truth of the matter is, those images are highly processed, they are displayed in a way that actually accentuates differences from one frame of the movie to the next. And therefore, those images actually can be misleading. What you need to do is to use those images to generate a hypothesis about what might be going on, and then go to the numbers and the curves to actually evaluate quantitatively what's happening.**

Q. **So even if the videos looked like Flonase was behaving differently than Nasacort AQ, would you agree that there is any difference between the two, given the data you have looked at?**

A. **No.**

Q. **Why not?**

A. **Because I think the statistical analysis, which is the more reliable approach to the data, shows that there was no statistically significant difference in the deposition or the clearance of Nasacort with AQ and Flonase.**

Q. **So in your opinion, have you seen any scientific data showing that there is a statistically significant difference between Flonase, the prior art product, and Nasacort AQ, in**

deposition or clearance?

A. **No. The combined data from the 1998 and the 2002 study do not show statistically significant differences, in my opinion.**

Q. **And finally, it was suggested to me that we might need to clarify an issue on the frontal sinus discussion we had.**

Will you please pull up demonstrative 43.

This is the demonstrative we looked at yesterday regarding the 1996 study?

A. **Correct.**

Q. **The lower right-hand cube that is highlighted there is the one we were discussing.**

A. **Yes.**

Q. **With the overlap with the frontal cavity?**

A. **Correct.**

Q. **Dr. Berridge, I think, testified that he would have assigned that cube to the frontal cavity rather than the frontal sinus in the 1996 study? Not that cube, but a cube like that?**

A. **I believe this is what he stated.**

Q. **If he did that, would his frontal sinus data be accurate?**

A. **No. His frontal sinus values would be underestimates of the true activity in the frontal sinus, if any were there.**

Q. **So in the 1996 study that was reported in the Journal of Nuclear Medicine, would the frontal sinus numbers be accurate in that journal article?**

A. **If he did what he said, then those numbers presented in the journal would be inaccurate, underestimates of the frontal sinus activity.**

Q. **Okay. And the frontal cavity data in the Journal of Nuclear Medicine article, would that data be accurate?**

A. **No. Those data would also be inaccurate. They would be slight overestimates of the activity in the frontal cavity.**

Q. **So given those facts, would you expect such a discrepancy to be described and explained in the article?**

A. **Yes, I would.**

Q. **If you could pull up Demonstrative 44.**

Did we prepare a demonstrative analyzing the data, the frontal sinus data from the three studies?

A. **Yes, we did.**

MS. BALDWIN: I am sorry. I have a concern.

THE COURT: Do you have an objection, counsel?

MS. BALDWIN: He was still under oath last night. If this is the demonstrative --

THE COURT: Counsel, you don't speak to counsel. You address the Court.

Let's talk at sidebar.

(The following took place at sidebar.)

THE COURT: Counsel, this is Federal Court.

MS. BALDWIN: I apologize.

THE COURT: What is your concern?

MS. BALDWIN: My concern is, we received a new demonstrative last night which I was not going to object to, except that counsel just made the representation that this was something they had worked on last night and the witness was still under oath. So I have some concerns if counsel was discussing his testimony with him last night.

THE COURT: You should.

MS. RURKA: Your Honor, we were just clarifying a point that we needed to make today during testimony.

THE COURT: But the witness is under oath. You are not supposed to discuss the witness' testimony with him or her who is under oath. It is a fundamental precept of trial practice, regardless of the courtroom you are in. You are certainly not going to do it in my courtroom. So what was discussed?

MS. RURKA: We just discussed the same data that we have been discussing all along. All we discussed was, we had looked at the data --

THE COURT: Here is what I am going to do. I am going to preclude this kind of inquiry.

MS. RURKA: I apologize, Your Honor.

THE COURT: I am going to give some thought to this. Beyond that, you don't need to worry about it. This is out. However else I may address the problem, we will leave that for another day.

(End of sidebar conference.)

THE COURT: You can take that down.

MS. RURKA: We have no further questions.

THE COURT: You may cross-examine.

MS. BALDWIN: Thank you, Your Honor.

CROSS-EXAMINATION

BY MS. BALDWIN:

Q. **Good morning, Dr. Siegel.**

A. **Hi, Allison. How are you. I hope you didn't stay up at night thinking of ways to beat me up today.**

Q. **Of course not.**

THE COURT: Let me see lead counsel and local counsel.

(The following took place at sidebar.)

THE COURT: Given what I just heard, I've got a real concern. I have ruled and you have now been told that that testimony is out of order given the admission that there was a conversation with a witness under oath about his testimony. Do you want to explain yourself?

MR. HURST: I take full responsibility. Because he was still on direct and there was point of clarification,

I thought that that was permissible.

THE COURT: No. You should have at least inquired of me as to whether I would permit that. I've had this happen many times where lawyers, they're not sure, and I will tell you that my practice is and local counsel will tell you that you can't.

MR. HURST: I have to explain. It's completely my fault. I take full responsibility, Your Honor.

THE COURT: Especially to put a young lawyer in that position.

MR. HURST: I didn't -- it didn't actually occur to me. That is the truth, it did not occur to me, Your Honor, because he was still on direct. It literally did not occur to me. It didn't occur to her either. I take full responsibility.

THE COURT: That's why I called you up here. After I thought about it, it's not fair for me to come down like a ton of bricks on Ms. Rurka.

MR. HURST: Please, I take full and total responsibility.

THE COURT: We'll talk about it later.

MR. HURST: Thank you, Your Honor.

THE COURT: And you can tell her I don't have a problem with her.

MR. HURST: I appreciate that. Thank you, Your

Honor.

(End of sidebar conference.)

BY MS. BALDWIN:

Q. So, Dr. Siegel I'd like to start the day talking about what you and Dr. Berridge actually agree upon.

A. Okay.

Q. So you and Dr. Berridge both agree that PET is the best nuclear imaging technique for this type of study when you are trying to detect the amount of drug deposited and retained inside the nasal cavity. Isn't that correct?

A. Currently available technologies, I think it is the best.

Q. And you guys both agree this is an accepted as an accurate technique for quantitatively measuring the amount of radiotracer in a region. Is that correct?

A. Yes, I agree with that statement, but, of course, the accuracy of the measurement depends upon applying the method directly when you are doing a particular experiment.

Q. And another folder of things you guys agree on.

You guys, you and Dr. Berridge both agree that Nasacort AQ deposited in the frontal cavity in the 1996 volunteers and was retained for about an hour. Correct?

A. Correct.

Q. You and Dr. Berridge both agree that Nasacort AQ deposited in the turbinate regions of the 1996 volunteers

and was retained for about an hour. Correct?
A. Correct.
Q. Okay. And you both agree that Nasacort AQ deposited in the maxillary sinus and was retained for about an hour in the 1996 volunteers. Correct?
A. That's what I stated, yes. I just would add the maxillary sinus numbers are rather lower so there potentially could be problems with the maxillary sinus numbers but I did say that.
Q. Are you changing your testimony?
A. No, I'm not.
Q. So your only point of dispute on the 1996 study data is whether or not Nasacort AQ deposited in the frontal sinus of the 1996 volunteers. Correct?
A. With respect to the '96 data.
Q. '96 data.
A. That's correct.
Q. Okay. So despite the fact as you just pointed out the maxillary sinus numbers were low, you don't dispute that that shows actually deposition and retention in the maxillary sinus of the 1996 volunteers. Correct?
A. I think it's a fair statement. I'm not disputing that. Although as I stated a moment ago, the potential for problems with the maxillary sinus data would be greater because the numbers are lower.

Q. **But you are not changing your testimony. Correct?**
A. **I am not changing my testimony.**
MS. BALDWIN: Could I have P Demo 154, please?
BY MS. BALDWIN:
Q. **Now, Dr. Berridge prepared this graph which is the 1996 data for all of the subjects for both of the frontal sinus and maxillary sinus. But you don't believe that the frontal sinus data is actual data or the maxillary sinus data in this graph is actual data. That's your position; right, Dr. Siegel?**
A. **That's correct.**
MS. BALDWIN: Thank you.
BY MS. BALDWIN:
Q. **Now, you mentioned yesterday that your primary research area in the industry use of PET is in oncology. Is that correct?**
A. **That's correct.**
Q. **In oncology PET work, the radiotracer is normally administered intravenously through a vein. Correct?**
A. **That's correct.**
Q. **It's not administered through inhalation?**
A. **That's correct.**
Q. **And you actually never conducted a PET scan on the nasal anatomy in your 30 years of experience in PET. Correct?**

A. That's correct.
Q. Nor have you conducted a study where you broke apart the regions of interest in as many different regions as Dr. Berridge did in his studies. Correct?
A. No, that's not correct. I have done some studies involving cardiac metabolism with several different traces where we decided the myocardium into many different adjoining regions. It's slightly different type of study but the same basic principle.
Q. You haven't --
A. Those were dynamic data, I would add, as well.
THE COURT: What does that mean?
THE WITNESS: Images not just acquired at one point in time but images acquired over a time sequence to look at the change in activity as a function of time.
BY MS. BALDWIN:
Q. That is a little inconsistent with what you told me just a few months ago when I asked you.
THE COURT: Do you want to ask a question and not argue with the witness?
MS. BALDWIN: I'm sorry.
THE COURT: You can make that argument at some point in your brief, certainly.
MS. BALDWIN: Yes, I promise.
THE COURT: Okay. I'm sure.

(Laughter.)

MS. BALDWIN: May I approach?

THE COURT: Yes, you may.

THE WITNESS: Just what I wanted, another copy of the deposition.

THE COURT: Counsel.

(Court and Ms. Rurka go to sidebar; off record.)

BY MS. BALDWIN:

Q. Dr. Siegel.

A. Yes.

MS. BALDWIN: Let's look at Page 74 of his transcript, please. And let's look at Line 23. And it goes on to 75, down to Line 5.

BY MS. BALDWIN:

Q. Now, you see that, Dr. Siegel?

A. Yes.

Q. Okay. I asked you a few months ago:

"Question: Have you ever had to -- have you ever done a study where you broke apart the regions of interest in as many different regions as this study was done?"

You told me:

"Answer: Personally, no."

A. That's what I'd said. But I have done, as I just indicated, not as many regions as this one but the cardiac

studies we have done in the past had more than a single region for the entire heart.

Q. **Have you ever used cubic regions of interest such as the ones used in this 1996 PET study by Dr. Berridge?**

A. **I have not.**

Q. **So you have never actually conducted a PET scan in the exact same manner as Dr. Berridge conducted his 1996 study, have you?**

A. **That's correct. As Dr. Berridge testified, he is really the only one that has done a study like this.**

Q. **Have you ever done a PET study where someone is in a vertical position for part of the study and then is put in a horizontal position?**

A. **I have not.**

Q. **As an expert in this case, have you conducted any PET studies of Nasacort AQ?**

A. **I have not.**

Q. **Did you conduct any PET studies of Barr's ANDA product?**

A. **I was not asked to.**

Q. **So you have no data of your own on whether or not either Nasacort AQ or Barr's ANDA product deposit in the frontal sinus. Correct?**

A. **That's correct.**

Q. **The only data we have is that, that was done by**

Dr. Berridge?
A. That's correct.
Q. But you had the capabilities to do so. Correct?
A. If I had been asked to do so, I could have done so.
Q. You weren't asked?
A. What?
Q. You weren't asked?
A. I was not asked to do those studies.
Q. Since you have never done a PET study using cubic regions of interest, you have never actually had to align an array of cubes over anatomical regions before. Correct?
A. I've not personally done it but I think I know how I would try to do it.
Q. But you have never personally done it?
A. That's correct.
Q. And you don't know whether or not there was any overlap between a cube assigned to the frontal sinus and one that was assigned to an adjacent region?
A. That's correct. As I indicated, the raw data are gone and there are no source documents to show us how those regions were actually assigned.
Q. If you had been faced with a situation like that, that had overlap such as the one shown in your demonstrative, would you have adjusted the array of cubes to minimize that overlap?

A. **I might have done it if it was of concern to me.**

Q. **And you heard Dr. Berridge testify how the technician could adjust that array of cubes in three dimensions in order to get the alignment as best possible within anatomical regions. Correct?**

A. **I heard him say that.**

Q. **So if you heard Dr. Berridge -- I apologize.**

If you had taken precautions to minimize the overlap, why do you think that Dr. Berridge would not have done the same?

A. **My basis for thinking that he might not have done the same is the fact that he did not report it in either his study report or his scientific publication. And in a publication where he makes the claim that as an unexpected finding we have found activity in the sinuses, and specifically in the frontal sinus. And if there was some measurement artifact related to how the cubes, as we just discussed, as to how the cubes were assigned to one region or another, that could have affected the frontal sinus measurement either in a positive or a negative way, I personally believe that that is important enough to disclose to the editor of a journal for public consumption and to disclose to the sponsor of the research so that they would understand what the numbers meant.**

Q. **Do you remember how many cubes there are for each**

volunteer?

A. There were 104 cubes, as I recall, in the array. 729 two-by-two-by-two millimeters, reassembled -- I take that back. Lots of two-millimeter cubes reassembled into 1.8-centimeter cubes, 104 of those.

Q. Your critique of that is for each of the volunteers in the 1996 study, Dr. Berridge did not specify where each of those 106 cubes was located in his 1996 paper?

A. So the answer to that question is, my critique is that there was a special result that came out of that study, which is the purported data in the frontal sinus, he had to make, according to his testimony, a special adjustment in the way he assigned the cubes such that it might lead to underestimation of the activity in the frontal sinus.

And I would think that that level of care would require reporting in the scientific literature, since the study result was indeed unexpected, as he said.

Q. But his article was peer-reviewed. Correct?

A. It was peer-reviewed.

Q. And it was published in a very respected journal?

A. It was published in a respected journal. But I think, as I told you in my deposition, that doesn't mean that points like this don't slip through the peer-review process. And not everything that is published in a journal, as you know, is correct. Journal results are retracted sometimes

because people find that they made mistakes. And the peer-review process is not perfect. It's been very carefully studied and shown not to be perfect.

Q. If something is called a surprising result, it seems like it would have alerted the reviewer of the article?

A. Perhaps, yes. And perhaps, not. Depending on the type of reviewer. As I suspect, and I don't know who reviewed that paper, I think as I told you, I did not, if the reviewers were primarily individuals involved in PET imaging just generically, physicists, other chemists, rather than experts in nasal anatomy and nasal sprays, they might not have picked up on the fact that this was an important finding to bring up in the review process.

The Journal of Nuclear Medicine back at that point in time was typically using only two peer reviewers for each article. It might go to additional peer reviewers if there was a conflict between the original two.

So depending on the luck of the draw, how the editor picked the reviewers, which of four reviewers might have been invited to review, actually agreed to review the article, you might or might not have that comment. I can tell you, in my own role as an associate editor, where I am responsible for selecting reviewers and looking at their reviews, I often find widely disagreeing views between individuals who I would have thought would have reached the

same conclusions.

So the process is not perfect.

Q. I understand that, Dr. Siegel. But despite all of your hypotheses that you have just given, the fact is that it was peer-reviewed and accepted and published. That's a fact?

A. As a pilot study, that's a fact.

Q. Let's talk about the demonstrative you put up yesterday, talking about potential sources of error for the 1996 PET study.

A. Okay.

Q. So alignment we have already kind of touched on about the cubes. I was surprised to see scatter on your list, because at your deposition, I asked you if the activity seen in the frontal sinus in the 1996 study was due to scatter. And you actually corrected me and said that you didn't believe it was due to scatter.

Has your position on that changed, Dr. Siegel?

MS. RURKA: Objection. Improper.

THE COURT: I will sustain the objection to the form of the question. Please rephrase, counsel.

BY MS. BALDWIN:

Q. We will look at the actual transcript.

MS. RURKA: I am going to object to this. It is still improper.

THE COURT: Are you trying to impeach him with a prior inconsistent statement? I think there is a way to do that.

MS. BALDWIN: Yes. I will do it.

THE COURT: All right.

BY MS. BALDWIN:

Q. **Look at Page 264 of your transcript.**

THE COURT: Let's see counsel.

(The following took place at sidebar.)

THE COURT: I want Ms. Rurka to state with specificity her objection.

MS. RURKA: I don't think he has made an inconsistent statement at his deposition. She hasn't established that.

THE COURT: That is her objection. I am sure you will be able to establish that.

(End of sidebar conference.)

BY MS. BALDWIN:

Q. **My apologies, Dr. Siegel.**

A. **Thank you. I had time to read what is on those pages.**

Q. **So at your deposition, I asked you if your analysis affirmatively told you --**

MS. RURKA: Objection.

THE COURT: Sustained.

BY MS. BALDWIN:

Q. **At your deposition, when I asked you about the issue of scatter --**

MS. RURKA: Objection, Your Honor.

THE COURT: Here is the point: In order to query him in this manner, you would have to establish that the statement that you are referring to, that there is some inconsistency in the prior statement and that which he has made today.

Maybe you could go back a little ways.

MS. BALDWIN: I sure will.

MR. BERGHOFF: May I approach the questioner?

THE COURT: Yes, you may.

(Counsel confer.)

THE COURT: Thank you, counsel.

BY MS. BALDWIN:

Q. **My apologies, Dr. Siegel.**

A. **No problem.**

Q. **Does your analysis of the 1996 frontal sinus data affirmatively tell you that the activity seen in the frontal sinus in 1996 was due to scatter and not to deposition in that region?**

A. **No. I don't believe I ever said that. I think what I said yesterday, and I think what I said in my deposition, was that scatter was another factor that could contribute to misinformation on a PET scan. When there is scatter,**

activity is put in a place where it is not really there, and you get a false measurement because of scatter. I think I said in this deposition that I thought with respect to the frontal sinus that overlap of the frontal sinus region with an adjacent region was likely the dominant factor responsible for the problem in the 1996 study, and scatter was potentially an additional contributory factor.

Q. Scatter is an issue with all PET studies. Correct?

A. That's correct.

Q. So that is a potential source of error across all three of Dr. Berridge's PET studies. Correct?

A. That's correct.

Q. And so that is a potential source of error that must be considered in the analysis of any PET study, not just the one conducted in 1996. Correct?

A. That's correct.

Q. You mentioned spillover on that list as well. Is spillover a potential source of error in all PET studies?

A. Absolutely, as I said yesterday.

Q. So this also is a potential source of error that encompasses all three of the PET studies conducted by Dr. Berridge?

A. Yes. But I think the spillover effect would be substantially greater with the cubic regions of interest abutted one right next to the other than it would be with

the contrary regions of interest used in the 1998 and the 2002 studies.

Q. **But this is a potential source of error that must be taken into consideration when designing any PET study?**

A. **That's correct.**

Q. **And someone with 30 years of experience in PET, like you and Dr. Berridge, would know to consider these potential sources of error when designing a PET study. Correct?**

A. **One would hope so. But as I said, we don't have the raw data left remaining to see what really was done in the 1996 study.**

Q. **Dr. Berridge actually did his graduate study work at Washington University in your department. Correct, Dr. Siegel?**

A. **In my department. But Dr. Berridge's graduate work was in radiochemistry, not in actually conducting PET studies.**

Q. **But we wouldn't doubt his training in PET, would we?**

A. **He has had experience in PET. I doubt if he actually had -- let me not say that. Let me say that I don't know how much actual training in performing PET studies and analyzing PET data he had during the course of his graduate training at Washington University, which was primarily in the preparation and synthesis of radioactively labeled drugs under the tutelage of Dr. Michael Welch, who is a chemist,**

not a PET imager, not a PET physicist.
Q. Let's talk about the 1998 versus -- the 1998 results graph that you put up. Could I have DX Demo 39.
Now, Dr. Siegel, the nasal cavity was the region of highest deposition in the 1998 study. Correct?
A. Correct.
Q. About 60 percent on this graph?
A. At peak, yes.
Q. And I think we are all in agreement that the frontal sinus was the region of smallest deposition in the 1998 study?
A. That's correct.
Q. Now, why did you graph the region of interest with the greatest amount of deposition on the same y axis as the region of interest with the smallest amount of deposition?
A. I think to try to show whether there was any similarity, these curves, because of the potential for overlap, spillover, scatter, the frontal cavity region, the nasal cavity region would likely be the area most likely to be contributing these problems to the frontal sinus.
Q. But if you graph any small value on a large enough scale, it's always going to look like zero, isn't it?
A. That's correct.
Q. We know from Dr. Berridge's graphs on Monday that those points are actually not at the zero line, don't we?

A. **Well, they are not precisely at zero. But they are not a whole lot over zero, no.**

Q. **They are not zero?**

A. **In the '98 study, they are not precisely zero for three of the five subjects. For two of the five they are virtually zero.**

Q. **Aren't zero or not zero?**

A. **That's a statistical question, rather than just -- we can do first-grade math or we could think about it statistically. If we have numbers that are varying up and down very close to the zero line, that's zero. But if you ask me, is .001 different from zero, you know what I would say. It's different. But that's first-grade math.**

Q. **During your testimony, you have relied a great deal on that 2002 study report. Correct?**

A. **Correct.**

Q. **And yesterday you also commented on the statement that Dr. Berridge made.**

Could you pull up PTX-351 for me, Eric. Page 10. Highlight that first sentence.

We talked a lot about this statement. This is a contemporaneous statement by Dr. Berridge, isn't it?

A. **What do you mean by contemporaneous?**

Q. **This statement was made at the time of the study. Correct?**

A. **Well, it was made at the time the study report was prepared, which was presumably sometime after the study was completed.**

Q. **This wasn't a document that was created as part of this litigation?**

A. **That's correct.**

Q. **Now, you read this statement when you reviewed the 2002 study report?**

A. **Correct.**

Q. **Did you specifically test or evaluate any other regions of interest apart from the frontal sinus to determine whether or not there were unusual variations in the data?**

A. **I relied on the investigator's own statistical analysis of the data that was included in this report.**

But I focused my observations on the frontal sinus because those were the ones that I was instructed to focus on by counsel and the ones that seemed to be most relevant to the case.

Q. **So you did not conduct that same analysis for the other regions of interest, just the frontal sinus?**

A. **I looked at the data. Are you asking me if I did a formal statistical analysis?**

Q. **Did you, for any other regions of interest?**

A. **I looked, for example, at the frontal cavity regions.**

I looked, for example, at the turbinate regions, and just looking at the general averages and the standard deviations, without doing formal statistical testing, did not think that the 2002 data, when we looked at those kinds of numbers, looks all that different from the 1998 data and from the '96 data in those regions.

Q. So you only focused your analysis on the frontal sinus?

A. I focused my analysis on the frontal sinus.

Q. Just a few more questions. We haven't talked much about the 1998 data but in forming your opinion regarding whether or not Nasacort AQ and Flonase exhibited similar behaviors, you reviewed the 1998 data as well. Correct?

A. Correct.

Q. And you relied upon that poster that we showed the other day.

MS. BALDWIN: Could you put up PTX-569.

A. Well, I partially relied on the poster and also the spreadsheet of the data that had the actual process results.

Q. But this is part of what you reviewed in forming your opinion. Correct?

A. Correct.

MS. BALDWIN: If you could highlight the results section there? Thank you.

Would you like a hard copy of this, Your Honor,

or could you see it?

THE COURT: No, I'm fine.

BY MS. BALDWIN:

Q. **Dr. Siegel, do you need a hard copy of it?**

A. **I can see this.**

Q. **So in reviewing this poster presentation, do you see where it starts the highlight: You would have read the Flonase deposition in oral cavity regions was higher. This, with observations below, may indicate a higher fluidity and movement of the product, since oral deposition does not take place directly.**

And then, at the beginning of the next paragraph, it says:

The kinetics showed a very striking feature in the Flonase curves between 45-60 minutes.

MS. BALDWIN: Eric, if you could pull out the graphs for me on the left-hand side on that poster? Yes, those right there.

BY MS. BALDWIN:

Q. **In that top graph there, Dr. Siegel, is that the striking feature in the Flonase curves between 45 to 60 minutes referred to in that paragraph above?**

A. **I believe that is what he is referring to.**

Q. **Do you have any opinion about this striking feature of Flonase?**

A. **Well, you can look at average curves like this. You can look at videos but we're missing some important things on these curves. We're missing the error bars that show what the standard deviation is from subject to subject. And I think what is more important is analyzing these results in a reliable statistical fashion to ascertain whether there really is or is not a significant difference in these curves despite the apparent difference in their shape.**

Q. **But you had the raw data these curves were generated from. Correct?**

A. **That's correct.**

Q. **So you could have analyzed that to determine whether or not this striking feature was of significance to you?**

A. **I could have done but was not asked to.**

Q. **So since you were not asked, you did not do it?**

A. **I paid attention to what I was asked to do.**

MS. BALDWIN: No further questions.

THE COURT: Redirect.

MS. RURKA: Just briefly, Dr. Siegel.

REDIRECT EXAMINATION

BY MS. RURKA:

Q. **Do you have sufficient knowledge and experience to analyze Dr. Berridge's data, not having done it yourself?**

A. **I certainly believe so.**

Q. **And the article, the 1996 study article, the Journal**

of Nuclear Medicine article, would a peer reviewer know how Dr. Berridge assigned the cubic regions of interest if it wasn't in his journal manuscript submission?

A. No.

MS. RURKA: Thank you.

THE COURT: All right. Thank you, doctor.

THE WITNESS: Thank you.

MS. RURKA: We call Dr. Daniel Klingenberg to the stand.

THE COURT: Okay

- - -

DEFENDANT'S TESTIMONY

... DR. DANIEL JOSEPH KLINGENBERG, having been placed under oath at 9:46 a.m. as a witness, was examined and testified as follows ....

- - -

MS. RURKA: May I approach the witness?

THE COURT: Yes, you may.

(Binders passed forward.)

DIRECT EXAMINATION

BY MS. RURKA:

Q. Will you please state your name for the record?

A. Daniel Joseph Klingenberg.

Q. And are you testifying today an as expert?

A. That's correct.

Q. **What is you're area of expertise?**

A. **My area of expertise is chemical engineering and rheology. Rheology suspensions.**

Q. **Dr. Klingenberg, could you talk a little bit about your educational background?**

A. **Yes. I received a B.S. in Chemical Engineering from the University of Missouri; and that was in 1985. I did a Master's of Chemical Engineering, University of Illinois. That was 1989. A Ph.D. from the University of Illinois in Chemical Engineering. That was in 1991, I believe. And Post-Doc at the University of British Columbia in Pathology and Physics.**

Q. **What is your current profession?**

A. **I'm a Professor in the Department of Chemical and Biological Engineering at the University of Wisconsin and I've been there since the end of 1991.**

Q. **What is your main area of research?**

A. **My main area of research is suspension rheology.**

Q. **Does that include viscosity measurements?**

A. **Yes, that includes things like measuring and interpreting viscosity suspensions.**

Q. **How much experience do you have in the area of rheology and viscosity measurements?**

A. **I've been doing this research ever since I've got to the University of Wisconsin, over 16 years ago. I also did**

viscosity testing as a student in college. So 20 years total.

Q. Do you teach courses at the University of Wisconsin?

A. Yes, I do.

Q. And do you do research there as well?

A. Yes, I do.

Q. Are you a member of any professional associations?

A. Pertinent to this case, I'm a member of the Society of Rheology. In fact, I'm on the Executive Committee of the U.S. Society of Rheology. The same group Dr. Prud'homme is in.

Q. Are you a published author?

A. Yes, I am. I have over 60 publications, mostly in the area of rheology and particulate suspensions.

MS. RURKA: Your Honor, I would like to proffer Dr. Klingenberg as an expert in rheology and viscosities.

MR. BERGHOFF: No objection.

THE COURT: The doctor is accepted as an expert in the area.

BY MS. RURKA:

Q. Were you asked to conduct a project in this case?

A. Yes, I was.

Q. What were you ask to do?

A. I was asked to analyze data on the recovery of the viscosity of Nasacort AQ and other nasal spray formulations.

I was also asked to measure viscosities of Flonase to see if the viscosity fell in the ranges stated in these patents.

Q. **Okay. And when you say recovery of viscosity, what do you mean?**

A. **I mean after a suspension has been sheared or shaken, the viscosity tends to build over time and we're looking at how long it takes for that viscosity to recover back to its unshaken value.**

Q. **And were those tests done on products discussed in this litigation?**

A. **Yes.**

Q. **Did you reach a conclusion about how long it takes a product like Nasacort AQ to recover its setting viscosity?**

A. **Yes. After looking at all that data, I concluded that it takes hours todays for the viscosity to recover back to its setting viscosity.**

Q. **Would the same conclusion apply to Barr Laboratories ANDA product?**

A. **Yes, I believe so, since they are very similar compositions.**

Q. **Okay. What is your conclusion based on?**

A. **My conclusion is based on analyzing a variety of data that has appeared in this case: Dr. Lochhead's data, data from Aventis on Nasacort AQ. And then my own testing on Flonase.**

MS. RURKA: Okay. Let's discuss Dr. Lochhead's data first. Could you pull up DX-362 at Page 9? And could you pull out the shear and setting viscosity numbers for batch number four, please?

BY MS. RURKA:

Q. **You recognize this data?**

A. **Yes.**

Q. **Okay. Can you explain the numbers for me?**

A. **Sure. They're in groups of three. And so in the rightmost side here, these three numbers are measures of the setting viscosities, the viscosity of this Barr product that has been sitting relatively undisturbed for I believe two days. And in between each measurement is a five minute rest period I believe.**

Then the bottom set of numbers here, these are again measures of the viscosity after the sample has been sheared on a, or shaken on a Burrell wrist-action shaker on five minutes at full speed. And then these measurements are made with I believe 30 seconds of rest in between each measurements.

Q. **Okay. What is the total amount of time between when the product was shaken and when the last shear viscosity measurement was taken here?**

A. **I believe Dr. Lochhead said that there is about a minute to get that first measurement and figure in the 30**

second rest time. I think it's three-to-four minutes total to that last measurement.

Q. Okay. So the bottom number is the last measurement he took?

A. That's correct.

Q. And has Barr's ANDA product recovered its shear viscosity in the amount of time, the three minutes it took from shaking to doing that last measurement?

A. No, the viscosity has barely changed from the initial value. It hasn't recovered up to this 600 range. In fact, it's got about 500 percent to go or six times. It increases six times to get back to that value.

Q. So what do these numbers suggest to you about the time it might take? Do these numbers suggest anything to about the time it might take to recover the setting viscosity?

A. It suggests it will take much longer than three to four minutes to recover back to the setting viscosity.

Q. Were these measurements done on a Brookfield viscometer?

A. Yes, they were.

Q. Did you hear Dr. Prud'homme testifying yesterday that a Brookfield viscometer might not be the appropriate way to measure the recovery of the setting viscosity of these products?

A. Yes, I heard that.

Q. **Do you agree with him?**

A. **I disagree. I think this is a reasonable way to measure the viscosity as it recovers.**

Q. **Dr. Prud'homme said that the viscosity measurement itself might disrupt the product so that the viscosity would keep going down every time you did the measurement. Do you agree this disruption would make enough of a change to make the recovery, the recovery data unreliable?**

MR. BERGHOFF: I'll object. Leading.

THE COURT: Yes. Sustained.

MS. RURKA: I apologize.

BY MS. RURKA:

Q. **Could you explain what your understanding of Dr. Prud'homme's testimony was yesterday?**

A. **My understanding of that testimony was that the actual measurement causes these numbers to be lower than they would have otherwise. I don't think that is true because if the shear actually caused this number to be that low, then they never would have been able to measure the setting viscosities. It would have destroyed those numbers as well and the numbers around 600 would have been down around 100.**

Q. **You also mentioned testing Aventis did. What was that testing?**

A. **That was also testing measurements of the viscosity of Nasacort AQ as a function of setting viscosity and then the**

recovery as a function of time after material had been shaken.

MS. RURKA: Could you please pull out DX-23 at Page 97?

BY MS. RURKA:

Q. Is this the data you are referring to?

A. This is the data.

Q. Was this testing done on Barr's ANDA product?

A. No, this is testing on Nasacort AQ.

Q. And could you just explain what these data are showing? Could you explain the columns?

A. Sure. The first column is just time. And then the second column are the viscosities measured at those various times. The first row here, this is the -- it says unshaken. And so these are measurements of the viscosity. It's the setting viscosity material. The material when it's relatively undisturbed.

Q. What sort of instrument were these measurements taken on?

A. This was taken on a Brookfield Viscometer.

Q. And why are the numbers, the shear viscosity numbers, so high?

A. The shear viscosity here, the setting viscosity up here at the top of about, average of 3500 centipoise for these two measurements are larger than what we see in Dr.

Lockhead's report because these are being measured at a much slower rotation rate. This is at six revolutions per minute as opposed to 30 revolutions per minute.

Knowing what we know about thixotropic fluids, these viscosities should be much higher.

Q. **What is the second row?**

A. **That second row just indicates the material was then shaken after that setting viscosity was measured.**

Q. **And how about the third row?**

A. **Then the third row is where they start measuring the viscosity as a function of time. Here we have at 30 minutes the viscosity average of two measurements is 330 centipoise. Then as time goes on you can see the viscosity increases. By the time you get to 24 hours down here, you can see that it's recovered to about 1500 centipoise, which is quite a bit to go yet to get up to the 3500 centipoise of the setting viscosity.**

Q. **Dr. Klingenberg, I think you said 30 minutes on that third row. Is that the right number? Is it 30 minutes after shear?**

A. **So this is immediately after shear, the viscosity is 330 centipoise. Down here at 24 hours after being shaken, the viscosity is around 1500 centipoise.**

Q. **Okay. How about at the bottom row, what is that showing?**

A. **It shows at 120 hours, which is about five days, they are still measuring viscosity below the setting viscosity. So this is about 2100 centipoise or so, which is still not yet two-thirds of the setting viscosity. It hasn't recovered yet even after five days.**

Q. **Okay. You also mentioned that you had conducted some testing on Flonase that supported your opinion that these compounds don't recover their setting viscosity. What did you do with Flonase?**

A. **Well, we sheared some Flonase, and then measured the viscosity of that Flonase using a Brookfield Viscometer, running at 30 revolutions per minute for 30 seconds. We did that measurement at several different times. And the viscosity after 30 minutes was still less than 50 percent of the setting viscosity.**

Q. **What does that tell you about Nasacort AQ and Barr's ANDA product?**

A. **Since these are all fairly similar compositions, this tells me that the viscosity of these products, after shaking, take hours to days to recover to their setting viscosities.**

Q. **Did you hear Dr. Prud'homme testify about the Hydan report the other day?**

A. **Yes, I did.**

Q. **What did you hear him testify about that report?**

A. **What I heard, which is consistent with his expert report, was that the Hydan report suggests the viscosity recovers to within 90 percent of its setting viscosity within 30 seconds.**

Q. **Can we pull up Plaintiffs' Demonstrative 43.1. Thank you.**

Can you just describe briefly what we are looking at here?

A. **Sure. This is a plot prepared by the plaintiffs, I believe, of the viscosity on the y axis here, measured as a function of time, for four different formulations. Nasacort AQ AZ3 is this orange curve here.**

Now, in this experiment, the material is being sheared pretty hard. For the first 30 seconds, that is a shear rate of 100 inverse seconds. Right here at 30 seconds the shear rate is rapidly decreased to one inverse second. Then the viscosity is then continued to be measured as a function of time.

Q. **Is this the Hydan report Dr. Prud'homme was talking about?**

A. **Yes. This is the Hydan report.**

Q. **What did Dr. Prud'homme testify about this? What is your understanding of what he was saying about this data?**

A. **My understanding is that he said that this data showed the viscosity recovered within 30 seconds, recovered to**

within 90 percent of its setting viscosity in 30 seconds.

Q. And what is he relying on in the data to show that?

A. I am actually not sure because I don't think it shows, respectfully, I think it doesn't show that it recovers rapidly, mainly for three reasons.

I think undue attention is paid to this jump. This jump, I believe, is not due to recovery but it's due to something else.

THE COURT: Which jump are you talking about?

THE WITNESS: The fact that the viscosity goes from this low number very rapidly up to this higher level, when the shear rate is decreased from 100 to one inverse second.

So it is from that level up to that level (indicating). That is one thing.

I think another thing, based on what we know from this other data we just described, recovery goes for a very long time, this experiment is stopped at 120 seconds, 90 seconds after the shear rate was stepped down to one inverse second. This just doesn't go long enough.

Also, I think that the magnitude of the viscosities are inconsistent with Dr. Lockhead's results.

BY MS. RURKA:

Q. Okay. So could you explain the jump, why you think the jump is not indicative of recovery, the jump in the data

from the zero to 30 time point and then from the 30 to 120 time point?

A. I will try to move my pointer, get it a little steady here.

So this jump from this line to this line, whether the shear rate is rapidly --

THE COURT: You say this line to this line, Doctor. Maybe you could describe it.

THE WITNESS: How about the orange lines, which is the data for Nasacort AQ, just for example here in this diagram.

This jump is actually expected to occur for thixotropic fluid even if there is no recovery at all, just because you have dropped the shear rate. We expect that to happen when there is no recovery.

So I don't think -- in fact, this jump is not due to recovery. This is just due to a phenomenon* for thixotropic materials.

BY MS. RURKA:

Q. And you also said this experiment is not being conducted over a sufficient amount of time. What do you mean by that?

A. Again, we see that the recovery of materials like this, in fact, there is other data from Aventis on the Nasacort AQ, this takes hours to days to recover. This

isn't nearly long enough to see the ultimate viscosity. In fact, I would say that it looks like these curves might be increasing with time. But it's kind of hard to tell, there is such a short window.

Q. You also mentioned that Dr. Lockhead's data supports your opinion. Dr. Lockhead conducted -- did he conduct testing using the same viscometer as was used here?

A. No. He measured the setting viscosity and shear viscosity, for that matter, of Nasacort AQ using a Brookfield Viscometer, Brookfield LVT Viscometer.

Q. What would the setting viscosity, if you were to translate Dr. Lockhead's results into the results on this different viscometer, what would the setting viscosity be?

A. Well, I would estimate, based on his results, measuring with the Brookfield at 30 rpm's, that for one inverse second, the setting viscosity should be around 4,000 centipoise.

I will point out that the units here on this axis, this is pascal-seconds, so this orange curve is sitting here at about .15 pascal-seconds, which is 150 centipoise. And I would estimate, based on Dr. Lockhead's results, the setting of the undisturbed viscosity we measure at one inverse second should be up at around 4,000 centipoise. Much, much higher than that.

Q. If you were to show recovery -- you know about the

setting viscosity of Nasacort AQ. If you were to show that Nasacort AQ in this graph were to show that Nasacort AQ recovered 90 percent of its setting viscosity within 30 seconds, where would the orange line be at 30 seconds to 120 seconds?

A. **That would be above the ceiling somewhere.**

Q. **And you got that it should be -- the setting viscosity should be 4,000 centipoise using Dr. Lockhead's data. Why?**

A. **Well, that is, again, he used a Brookfield Viscometer operating at 30 revolutions per minute from which I estimate the shear rate was ten inverse seconds. This is one inverse second. So I multiply his viscosity by ten to predict the viscosity of these shear fluids. When you decrease the shear rate down to one and take his number of a little over 400 centipoise, and you get 4,000 centipoise at this lower shear rate.**

Q. **So you multiply the 400 by ten?**

A. **That's correct.**

Q. **Dr. Prud'homme also relied on the FMC report.**

Could we first pull up PX-380 at Page 1.

Did you hear Dr. Prud'homme testify about the FMC report?

A. **Yes.**

Q. **And what was your understanding of what he was saying about this report?**

A. **My understanding was that he agreed with the highlighted sentence, that the high level of thixotropy* in the case in structure will go quickly after spraying.**

Q. **Does this sentence give you sufficient information to conclude that a product like Nasacort AQ would recover its setting viscosity in a short period of time.**

A. **No, it doesn't.**

Q. **Why not?**

A. **If you look at the data in this report, the data clearly is thixotropic. But they show little or no recovery. Furthermore they don't give you any indication of how long the experiments were performed. So even if there was recovery, you wouldn't be able to estimate a recovery time.**

Q. **You also mentioned that you had conducted -- so I guess in your opinion, do these materials recover their setting viscosity in about -- did they recover 90 percent of their setting viscosity within about 30 seconds?**

A. **No. They take hours to days to recover 90 percent of their setting viscosity.**

Q. **You also mentioned that you conducted some viscosity measurements on Flonase?**

A. **I did, yes.**

Q. **What were the results -- what were you asked to do on the viscosity measurements?**

A. **I was asked to measure the setting and shear viscosities of Flonase, as described in the patent, and to see if they fell within the ranges. And I was also asked to determine whether or not Flonase eventually recovered its setting viscosity after being shaken.**

Q. **What were the results of your testing on Flonase?**

A. **For Flonase, the setting viscosity was measured between 530 and 589 centipoise. The shear viscosity was determined to be 165 and 206 centipoise.**

Q. **So does the setting viscosity of Flonase fall within the claimed range of about 400 to about 800 centipoise?**

A. **Yes, it does.**

Q. **Does the shear viscosity fall within the claimed range of about 50 to about 200 centipoise?**

A. **Yes, it does.**

Q. **Dr. Lockhead criticized -- did you read Dr. Lockhead's rebuttal report in this case?**

A. **Yes, I did.**

Q. **Did he criticize your results in this case?**

A. **Yes.**

Q. **Did you review those criticisms?**

A. **Yes, I did.**

Q. **Are those criticisms, are they valid?**

A. **I don't believe so.**

Q. **Do you and Dr. Lockhead agree on any of the results in**

this case?
A. Yeah. I think we agree on the setting viscosities. I think we both got the same -- that we both agree that the setting viscosities are in the range specified in the patent.
Q. Did he agree with you on your conclusions on the shear viscosities falling within the range?
A. No. He measured larger shear viscosities than I did. His were outside the range. Mine was inside the range.
Q. Have you ever worked with nasal spray products like this before?
A. No.
Q. Do you have a general approach to measuring, conducting viscosity measurements on unfamiliar materials?
A. Well, when you get a material you haven't studied before, you need to examine it. You need to do some experiments, just to figure out what operating conditions, what parameters need to be set on the rheometer. So you need to do a little bit of investigation first.
Q. Did you do some investigation with Flonase when you were received it?
A. I did, yes.
Q. When you received it, how did you go about measuring the shear viscosity of Flonase?
A. Well, I started by trying to follow the description of

the measurements in the patent.

Q. Could we please pull up PTX-1 at Page 7.

Is this the description you read?

A. That's correct.

Q. Did this tell you -- did this give you sufficient information to measure the shear viscosity of Flonase?

A. No, it didn't. I believe there is information missing in this description.

Q. What information is missing?

A. There is quite a few things. I think most importantly for this case, for the shear viscosity, are the conditions for the shaking step.

Q. What sentence are you looking at for how to conduct the shear viscosity?

A. I am looking at the last sentence, where it says the shear viscosity is measured by mixing at 30 rpm for 30 seconds after mixing in a Burrell wrist-action shaker at full speed for five minutes.

Q. The Burrell wrist-action shaker, the mention of the Burrell wrist-action shaker didn't tell you how to conduct the shaking for the viscosity testing?

A. No. I think there is information missing, most notably, how full the containers need to be on the Burrell wrist-action shaker.

Q. Why is that important?

A. **Well, as a rheologist, I interpret this passage of this person trying to teach us how to characterize the viscosity or the thixotropy* of the formulations. For example, the setting viscosity characterizes the behavior of the material when it's been disturbed as little as reasonably possible. And the shear viscosity is characterizing the material when it's been deformed or shaken, as much as reasonably possible, with the equipment available.**

Now, how much deformation goes on during the shaking will depend on how full the container is that you are shaking.

Q. **Did you hear Dr. Prud'homme's testimony about ketchup up being thixotropic?**

A. **Yes. That was a good example. We have all had the experience with a full bottle of ketchup. It is very hard to shake that up and get the ketchup to pour out. It is much easier to shake up and then pour a half-filled bottle of ketchup.**

Q. **How did you determine how full to make the container that you were shaking?**

A. **Well, I started by taking 500 milliliter Erwin Myer* flasks and filling them halfway up. So 50-percent full, and putting those on the shaker for five minutes.**

Unfortunately, that turned my sample of Flonase

into foam Flonase. So I no longer had the material I wanted. I had a different material than regular Flonase.

Q. What sort of numbers did you get when you measured the viscosity of the foam?

A. Those viscosities were significantly higher, as expected, than what we ultimately determined to be the shear viscosity of those materials.

Q. How full did you determine that the container should be ultimately?

A. By doing some experiments, we found that filling these containers, these Erwin Myer flasks, 80-percent full, would allow significant deformation of the material when it was shaken. But it didn't produce too much foam so that we couldn't make the measurements.

Q. Okay. And after shaking it, did you conduct the shear viscosity measurements?

A. Yes, we did.

Q. Did you conduct the shear viscosity measurements in accordance with what is stated in the patent?

A. I believe so.

Q. Did you use the Brookfield Synchro-Lectric Viscometer?

A. I used a Brookfield LVT Viscometer.

Q. And you say LVT. Does that make a difference?

A. No, it's the same viscometer essentially. The only difference is the readout isn't an LED, a digital readout as

opposed to a dial readout but it's the same spring, same inner-workings, same thimbles.

Q. **Did you get the same measurements?**

A. **You get the same measurements, yes.**

Q. **Did you measure the viscosity at 20 degrees Celsius?**

A. **Yes, plus or minus half a degree C.**

Q. **Did you shake the sample on a Burrell wrist action shaker at full speed for five minutes?**

A. **Yes.**

Q. **And did you measure the shear viscosity by making at 30 RPMs for 30 seconds on the Brookfield?**

A. **Yes.**

Q. **Dr. Lochhead criticized some aspects of your shear viscosity testing. Did you read it that he criticized you for not using a 600 milliliter beaker to conduct the viscosity testing with the Brookfield?**

A. **Yes. That was my fault. I described in my reports that I used a 500 milliliter beaker. But it's actually a 600 milliliter beaker. I just referred to it as a 500 milliliter beaker because 500 milliliters is the largest labeled gradation on the side of the beaker so I called that a 500 milliliter beaker but the capacity is actually 600 milliliters. It's a 600 milliliter low foam beaker.**

Q. **And he also says you didn't use sufficient sample to actually measure -- the Flonase, the prior art product, the**

Flonase sample to measure the viscosity. Did you use the sufficient sample to measure the viscosity?

A. **Yes, there was no problem immersing the spindles to the indentation in the shaft.**

Q. **He also criticizes you for pouring sample after you shook it from an Erlenmeyer flask into the beaker where you were using the Brookfield viscometer. Did pouring it have any effect on the results in your shear viscosity measurements?**

A. **We did a few experiments to show that pouring had negative effect on the shear viscosity measurements.**

Q. **Did you put those experiments in your lab notebook?**

A. **Yeah.**

Q. **And were they produced to the other side, the lab notebook?**

A. **Yes.**

Q. **So whose results do you think are a better characterization of the shear viscosity of the prior art product?**

A. **With all due respect to Dr. Lochhead, I think this volume is an important parameter, and I think I did the experiments to determine what volumes are reasonable. And so I think our experiments for the shear viscosity are more reliable.**

Q. **What do you think explains the difference in your**

results?

A. **I don't know. I wasn't there when he did those measurements. Two possible explanations were that he didn't have sufficient air above the sample; the volume, containers were too full and therefore didn't get enough deformation perhaps. Perhaps there was foam that would lead to high her viscosity values. I don't know. Those are two possible explanations.**

Q. **Finally, you have seen Dr. Lochhead's viscosity test. Have you seen Dr. Lochhead's viscosity testing on Nasacort AQ and Barr's ANDA product?**

A. **Yes, I have.**

MS. RURKA: Could you please pull up Plaintiffs' Demonstrative 65?

BY MS. RURKA:

Q. **Do you know how much of a difference between shear viscosity numbers for Nasacort AQ and Barr's ANDA product? Do you know what the percentage difference is between the two?**

A. **So the average here is around 65. The average here is around 100. And so these, these numbers here on average appear to be about 50 percent larger than the shear viscosity of Nasacort AQ.**

Q. **Could a difference like this make a difference in how the product perform?**

A. **It could, I suppose.**

Q. **Have you seen any testing in this proceeding on Barr's ANDA product that showed how this difference would affect whether the product hits the frontal sinus?**

A. **No.**

MS. RURKA: I have no further questions.

THE COURT: All right. Counsel.

Mr. Berghoff. You may cross-examine.

CROSS-EXAMINATION

BY MR. BERGHOFF:

Q. **Good morning, Dr. Klingenberg. I'm Paul Berghoff.**

A. **Nice to meet you.**

Q. **Nice to meet you as well. I'll ask you some questions about your testimony. And perhaps about your expert reports that you filed in this case.**

A. **Okay.**

Q. **Now, you testified a bit this morning about some viscosity testing done by Aventis, not by Dr. Lochhead but by Aventis on Nasacort AQ. Do you recall your testimony?**

A. **Yes.**

Q. **And you're aware that that testimony was done using a Brookfield viscometer at a rotation speed of 6 RPM?**

THE COURT: Testing was done.

MR. BERGHOFF: The testing was done. I must have misspoke. That's what I meant to say.

THE COURT: Okay.

BY MR. BERGHOFF:

Q. **The Brookfield testing was done at a spindle speed of 6 RPM?**

A. **Yes.**

Q. **And the patent specifies that the testing speeds for both setting and for shear viscosity should be done at 30 RPM. Is that correct?**

A. **That's correct.**

Q. **Now, you were here when Dr. Prud'homme testified yesterday?**

A. **Yes.**

Q. **And do you recall or understand that Dr. Prud'homme testified that Brookfield, it has been called tabletop testing, is not the appropriate way to measure the recovery of the sheared Barr ANDA product or Nasacort with respect to its deposited form in the nose?**

A. **Yes, I heard that testimony.**

Q. **And that was just my question.**

And I get the impression from your testimony this morning that you believe that the so-called tabletop method, just seeing if the material sitting in a beaker recovers and how fast it recovers its viscosity is the appropriate test?

A. **I believe with current technology, that is the only**

choice we have to try to characterize the recovery.
Q. And you are testifying here on behalf of the defendant Barr?
A. That's correct.
Q. And so it goes without saying that you had full access to samples of Barr's ANDA product for testing?
A. (Shrugs shoulders.)
Q. You understand all you had to do was ask, Dr. Klingenberg, and they would give you samples of their product?
A. I suppose that is true. I don't know.
Q. And yet, believing that this tabletop methodology is the best way to determine recovery of viscosity, you never did that test on Barr's ANDA product, did you?
A. I did not, but the compositions are very similar so I expect to see the same recovery for the Barr's product.
Q. But the best proof of the pudding would have been actually doing the test on Barr's ANDA product, would it not?
A. Yes, I wouldn't expect anything different.
Q. Now, you testified about the Hydan report. And we've heard a bit about that in court from several witnesses?
A. Uh-huh.
Q. And you understand that that was a report prepared for Agis, the developer of Barr's product?

A. **Yes.**

MR. BERGHOFF: Could we put up on the screen, DTX-76?

And I believe, I believe that is in your binder, Dr. Klingenberg, but if not, I'll try and get you a copy.

And let's go to the second page.

Do you see the second, the second paragraph -- and perhaps we could blow that up -- Controlled Stress Rheometer, Viscosity Recovery, (Figure 2).

BY MR. HURST:

Q. **Do you recognize that this Figure 2 is the same figure from the Hydan Report that you were testifying to this morning?**

A. **Yes.**

MR. BERGHOFF: And let's just see what the Hydan report says about the recovery of viscosity. Could we highlight the sentence, third sentence that says the graph shows that? A little further up. We're getting there. Okay. Thank you, Eric.

BY MR. BERGHOFF:

Q. **I'm correct, am I not, that the Hydan report states that the graph -- refers to figure 2 -- shows that the viscosity recovers almost immediately to a constant viscosity in samples AZ2A, AZ3A and AZ4A. Do you see that?**

A. **I do see that.**

Q. **And sample AZ3A, could you confirm for me, that that is in fact Nasacort AQ?**

A. **I believe that is Nasacort AQ.**

Q. **So the contemporaneous evaluation in the Hydan report, this report for Agis, was that viscosity of Nasacort AQ recovers almost immediately to a constant viscosity. Correct?**

A. **I agree that the plot shows it's almost constant but I don't think it is the setting viscosity that it's recovering to and it's not recovery, it just has increased only so much during that period.**

Q. **So you disagree with Dr. Prud'homme's evaluation and with this statement in the Hydan report?**

A. **To the extent that this constant viscosity is the setting viscosity, yes, I disagree with the statement.**

Q. **Let's talk about your testing now, testing that you actually did. And all of that testing, as I understood it, was on Flonase?**

A. **That's correct.**

MR. BERGHOFF: May I approach, Your Honor?

THE COURT: Yes, you may.

BY MR. BERGHOFF:

Q. **I'm going to hand you, Dr. Klingenberg, what we have marked as Plaintiffs' Trial Exhibit 1057.**

(Exhibit passed forward.)

Q. **Do you recognize this document, Dr. Klingenberg?**
A. **Yes.**
Q. **And could you tell us what it is?**
A. **So counsel contacted me to see if I would be willing to act as a consultant expert witness in this case. And I prepared this document, trying to prove I could measure the viscosities in question in this patent so that they would hire me, basically.**
Q. **And it worked.**
A. **Yes.**
Q. **They did hire you.**
A. **Be careful what you wish for.**
Q. **Truer words were never said.**
What is the date of this document, Dr. Klingenberg?
A. **It says November 28th, 2007.**
Q. **And so at this point, you hadn't done any testing on viscosity of any samples for this case.**
A. **That's correct.**
Q. **I read through this document, and tell me if my characterization is fair or not. That this is a description at least in part of the protocol that you intended to use should you be used to test materials for this case?**
A. **Yes, I would say that in this document, I outline some shortcomings in the description of the patent and this is**

how I would proceed to overcome those deficiencies in the description of the patent to measure the viscosity in question.

MR. BERGHOFF: Let's go to the second page.

And I don't think we need to highlight anything.

BY MR. BERGHOFF:

Q. This refers to, in your document, the protocol using a Brookfield viscometer?

A. Yes.

Q. And then we have a section immediately beneath it that discusses the protocol for measuring the setting viscosity using the Brookfield viscometer. Is that correct?

A. Uh-huh.

Q. And then if we turn the page, so now page three of this exhibit, we get to the section on how to measure shear viscosity using the Brookfield viscometer?

A. That's correct.

MR. BERGHOFF: And if we could pull up the section, Eric -- yes, that's fine. And starting with the second paragraph.

BY MR. BERGHOFF:

Q. This document describes a method for determining the shear viscosity as follows:

Am I correct so far, Dr. Klingenberg?

A. Yes, it's almost what the phrase is.

Q. **I think I left and "as" out just for grammar. And there are three steps that follow. Is that correct?**

A. **That's correct.**

Q. **And the first step is the shaking step on the Burrell wrist action shaker?**

A. **Correct.**

Q. **And you propose shaking it as full speed for 5 minutes?**

A. **That's correct.**

Q. **And the second step is to immediately transfer a sufficient amount of this material. Is that the material you just shook?**

A. **That's correct.**

Q. **To immediately transfer a sufficient amount of this material to the container described above for the viscosity measurement?**

And maybe you can save us some time. What is the container described above in the document?

A. **That's a 500 milliliter beaker or, rather, an 600 milliliter low foam beaker.**

Q. **You called it a 500 milliliter beaker but it's really 600?**

A. **That's correct.**

Q. **Fair enough. And then the third step in your stated protocol here is to measure the viscosity using the**

Brookfield digital viscometer using a rotation speed of 30 RPM. Is that a correct reading and understanding of the third step?

A. **Yes.**

Q. **And you will allow the spindle to rotate for 30 seconds before recording the viscosity? Again, is that a correct understanding?**

A. **Yes.**

MR. BERGHOFF: And then the last sentence, if we could highlight that.

BY MR. BERGHOFF:

Q. **It says: Following Kim -- and then there are two citations -- this viscosity is the shear viscosity.**

That's what you stated in this document; correct?

A. **Correct.**

Q. **And without going to the footnotes in the back, the "Kim" you are referring to are the two patents in suit?**

A. **That's correct.**

Q. **So this states that these, this protocol is going to be the stated Kim shear viscosity protocol from the patents?**

A. **I think the next paragraph explains that you need to do some work to figure out what volume to put in the Burrell wrist action shaker step.**

Q. **Let's turn to your work. That's a good segue.**

I believe you have Plaintiffs' Trial Exhibit 447 in your book, or a copy of it? It's your handwritten notes reflecting your work.

A. **I'm sorry. What was the number again?**

Q. **My apologies. I will approach.**

A. **It might be here.**

Q. **It's easier for me to just hand it to you. I was wrong in assuming that you had it.**

Now, you have before you Plaintiffs' Trial Exhibit 447.

Could you confirm for us what this is?

A. **Yes. This is a photocopy of my lab notes from this project.**

Q. **Was this actually recorded in a laboratory notebook, Dr. Klingenberg?**

A. **This was recorded on a pad of paper.**

Q. **I believe in your testimony this morning you referred to recording your test results in a laboratory notebook?**

A. **It's a pad of paper, yes.**

Q. **You misspoke this morning?**

A. **Yes, I suppose so.**

Q. **And, indeed, you instruct your students to always record their experimental results in laboratory notebooks, don't you?**

A. **I wouldn't say I instruct them to always record in a**

laboratory notebook. But I do encourage them to do that and I tell them if they are going to go out in industry, this is important for them. But this has worked fine for me until this case.

Q. **So it is the best practice to record in a laboratory notebook your test results?**

A. **It certainly can't hurt.**

Q. **And this is your handwriting throughout on this document?**

A. **No. I was taking this opportunity to train a graduate student in measuring viscosities. And he actually wrote a few lines in here, in this document.**

Q. **There is a substantial portion of the document that is in your handwriting?**

A. **Yes.**

Q. **Please, if significant, feel free to point out where it's not in your handwriting. I am not trying to confuse that issue.**

Let's look on the first page. There is reference to two dates there, December 10 and December 11. That is of last year, I assume?

A. **That's correct.**

Q. **And am I right that there is some reference to doing some setting viscosity measurements on this first page?**

A. **Yes. I would view the first several pages of this as**

doing the exploratory work to figure out how to conduct the setting and the shear viscosity measurements.

Q. Let's see what you did. The first page is setting viscosity?

A. Yes.

Q. Let's go to the second page. The top two-thirds of this page is still setting viscosity measurements?

A. They are viscosity measurements, yes.

Q. Well, let me -- let's blow up the bottom third. Is that the first, from the word shear viscosity down, is that the first shear viscosity test you conducted, Dr. Klingenberg, in this case?

A. Yes, that is the first failed attempt, first attempt, the first failed attempt at measuring shear viscosity.

Q. And you shook that sample on a Burrell wrist-action shaker for five minutes at full speed?

A. That's correct.

Q. You measured its viscosity using a Brookfield Viscometer with a spindle speed of 30 rpm?

A. Yes. Technically, that's not Flonase anymore. That's Flonase plus air measuring.

Q. The spindle rotated for 30 seconds?

A. That's correct.

Q. And the viscosity measurement you got was 366 centipoise?

A. **That's the correct viscosity of Flonase plus air, yes.**

Q. **And you are aware that Dr. Lockhead has measured the shear viscosity of Flonase in this case?**

A. **Yes.**

Q. **You have reviewed his expert report that reports his results?**

A. **Yes.**

Q. **And he reports results for the shear viscosity of Flonase between 307 and 375 centipoise?**

A. **That sounds accurate.**

Q. **And so this viscosity, shear viscosity measurement that you obtained for Flonase is right in the range that Dr. Lockhead found?**

A. **This is viscosity for foam Flonase. This is Flonase plus air.**

Q. **And at the time you were doing this testing for Barr, you were aware that the range for shear viscosity stated in the patents in suit was 50 to 200 centipoise. Correct?**

A. **Yes.**

Q. **Let's go onto the next page, Dr. Klingenberg, of this exhibit, which is PTX-447. I need to be on Page 3. Yes.**

We are on a different day now. This is now December 12th of last year?

A. **Yes.**

Q. **And we have a report here of three setting viscosity**

measurements on this page?

A. **On this page, we have -- no, that's not accurate.**

Q. **Let's go through them.**

A. **Okay.**

Q. **Let's just pull up, if we could, Eric, the first box down to that first measurement there.**

You emptied 37 bottles, this is of Flonase?

A. **That's correct.**

Q. **Into a 500-milliliter flask. There was some foam on the top, you placed a stopper, no air, shook it for five minutes in a Burrell wrist-action shaker?**

A. **Correct.**

Q. **Was that at full speed?**

A. **Yes.**

Q. **You transferred it to a 500-millileter beaker. Correct?**

A. **Yeah.**

Q. **And then you measured the viscosity according to the protocol in the patent, Brookfield Viscometer, spindle speed. Correct?**

A. **We moved the spindle speed, at 36.9 at 30 seconds. And 36.5 at 60 seconds.**

Q. **You recorded a viscosity of 369 centipoise?**

A. **That's correct.**

Q. **And that's within the range that Dr. Lockhead found**

for this same material, Flonase?
A. I believe you started this by saying this was the setting viscosity.
Q. Then I misspoke. This is the shear viscosity?
A. Right, this is the exploratory work to try to figure out how to measure shear viscosity.
Q. This is shear viscosity because you shook it on the Burrell wrist-action shaker?
A. I would say I am still trying to figure out how to perform the experiments described in the patent at this point.
Q. And the result you got for shear viscosity here, 369 centipoise, is within the range that Dr. Lockhead found for Flonase. Correct?
A. Except that I wouldn't call this the shear viscosity as defined in the patent. This is a viscosity measurement.
Q. And it's above the 200 top limit of the range described in the patent for shear viscosity?
A. Yes. This viscosity, which is not shear viscosity, is above the 200-centipoise limit.
Q. Let's go to the second experiment reported on this page this says you shake another five minutes in flask?
A. Yes.
Q. Am I correct in understanding that now you have taken the same sample that you shook for five minutes at full

speed on a Burrell wrist-action shaker. And you now shake it another five minutes on a Burrell wrist-action shaker?

A. That's correct. Trying to figure out -- trying to understand how this material behaves, yes.

Q. So now we have a total of ten minutes of shaking of this sample?

A. That's correct.

Q. And the viscosity, as you recorded it, using the protocol in the patent, Brookfield Viscometer, 30 rpm, 30 seconds, is 30031 centipoise. Correct?

A. I would disagree that -- I am still trying to figure out how to carry out the protocol at this point.

Q. In fact, this isn't the protocol in the patent because you have shaken the sample for ten minutes?

A. Yeah. As I have said, this is exploratory work, trying to understand the sample. This is not attempting to follow the protocol at this point. I am trying to figure out how this material behaves.

Q. Let's look at the next experiment on this page. I believe it's at the bottom now. It's the third measurement you have taken on this day.

You shake the flask for another 15 minutes. So am I correct that we are now up to 15 minutes of shaking for this sample on a Burrell wrist-action shaker at full speed?

A. This is another five minutes, so a total of 15, yes.

For this exploratory part of the project, yes.

Q. **Thank you for correcting me.**

And the viscosity of this sample was 280 centipoise?

A. **That's correct.**

Q. **And that's above the patent range stated of 50 to 200 centipoise. Correct?**

A. **That number is above 200, I agree.**

Q. **And let's turn to the next page, and highlight the top third, if we could. Am I right in assuming that this is the fourth experiment on the day that was recorded, on the last page, December 12.**

A. **Yes.**

Q. **And you shake again the same flask, if I understand your notations. But you will correct me if I am wrong, you shake the same flask again for another five minutes. So we are now up to a total of 20 minutes at full speed on a Burrell wrist-action shaker. And the viscosity you record is 273 centipoise. Am I correct?**

A. **That's correct, yes.**

Q. **And that, even with 20 minutes of shaking on the Burrell wrist-action shaker at full speed is still well above the patent range of 50 to 200. Correct?**

A. **I am sorry, I didn't hear the question.**

Q. **I didn't add the "correct" at the end.**

A. **Yes. Again, I am is still exploring how to fill in the blanks in the patent.**

Q. **Dr. Klingenberg, your counsel will come back on redirect, I am sure, on this point.**

Now, starting at the bottom two-thirds of this page, on December 14 -- I don't think we need it blown up -- but am I correct that you start a series of what I will call impeller tests?

A. **Yes.**

Q. **And what is an impeller? What were you doing here?**

A. **So, again, I am trying to figure out how this material behaves. So I am having trouble shaking the material without getting foam. So I am trying to see if I can deform the material some other way. I am trying myself. I am not trying to follow the protocol. I am trying to fill in the blanks in the protocol.**

I think you asked what is an impeller. That is just a long shaft with basically a propeller-looking thing on the bottom.

You connect that to a motor. And you can stir the sample, just a stirring device.

Q. **And that -- I think you already answered this, but I just want to be sure -- use of an impeller to stir the material before testing its viscosity is not what's contemplated by the patents in suit?**

A. **Yes. Again, I am trying to learn about the material at this point.**

Q. **And your goal with this impeller testing was to try and determine what should be expected out of the shaker, the Burrell wrist-action shaker, because so far you haven't been able to obtain a sample that you could use. Is that correct?**

A. **Could you please say that again?**

Q. **I will be happy to. Your goal, Dr. Klingenberg, with the impeller testing, was to try and determine what should be expected out of the shaker, because so far you hadn't been able to obtain a sample that you could use?**

A. **I think that is fairly accurate, yes. I am trying to figure out if it's even possible to shear this material without producing foam.**

Q. **And you couldn't use any of the results you had so far, Dr. Klingenberg, because they were all above the patent range of 50 to 200. Correct?**

A. **Well, I know for a fact that the volume of air space above the sample in an Erlenmyer flask, when you shake it, is going to dramatically affect how much deformation the material gets. And so I know that I can vary the amount of deformation in the material by changing that volume. What I don't know is can I do it without foam.**

Q. **Let's look at, let's have you look at Page, at the**

page from December 18 in your handwritten lab notes here. That's on Page 6.

It looks like the results from that day run on for about four or five pages in this exhibit. Is that correct?

A. Yes, that sounds about right.

Q. And is it fair to say you were varying the amount of material in the container you were shaking, and then measuring the shear viscosity afterwards, on this day's work?

A. That's correct.

Q. Let's put up a demonstrative exhibit. I believe it's KG-1.

This is, just for simplistic purposes and speed of cross-examination, rather than walking you through each one of these, I would like you to confirm for me, or point out where there is a problem, that this graph accurately summarizes the shear viscosity numbers that you measured on December 18.

A. Again, I would not call these shear viscosity measurements. I would call these viscosity measurements, mainly because, for example, as you go from 232 to 206, et cetera, that's the same sample that's being shaken approximate multiple times. So this is not the shear viscosity.

THE COURT: We are going need to clear counsel table at this point. We will resume your testimony in a bit.

(Recess taken.)

THE COURT: Please be seated.

All right. We'll continue. Doctor, wherever you are.

I apologize we had to clear the courtroom but apparently we needed to seal that proceeding.

Okay. Mr. Berghoff.

MR. BERGHOFF: Thank you, Your Honor.

Let's put up Demonstrative Exhibit KG-1 again.

BY MR. BERGHOFF:

Q. **And just to reorient ourselves, Dr. Klingenberg, we're speaking about your testing reflected in PTX-447 on December 18th. It seems to run from Pages 6 to 10.**

And does our demonstrative exhibit that we've put up accurately reflect the viscosity values that you obtained on this day with different percentage capacities of material in the flask you were shaking?

A. **Yes. These are viscosity measurements of the sample I shook, different volumes in the container. That's true.**

Q. **And just so the record is clear, when the flask was about 100 percent full, you got a reading of 268 centipoise. Correct?**

A. **Yes.**

Q. **At 95 percent full, you got a reading of 232 centipoise. Correct?**

A. **That is correct.**

Q. **At 90 percent capacity, you got a reading of 206 centipoise?**

A. **That is correct.**

Q. **At 85 percent, now for the first time you are under 200 centipoise at 191 centipoise?**

A. **That is correct.**

Q. **And at 80 percent, you recorded a measurement on this date in your lab notes of 188 centipoise?**

A. **That is correct.**

Q. **And just so we're clear on the methodology, the first sample at 100 percent was shaken for a total of 5 minutes?**

A. **That's correct.**

Q. **The 95 percent sample was shaken for a total of 10 minutes?**

A. **That's correct.**

Q. **Fifteen minutes for the 90 percent sample?**

A. **My math has just left me but, yes, a five-minute progression. Sure.**

Q. **15 for 90 percent, 20 for 85 percent, 25 total minutes on the Burrell wrist action lake for the 80 percent sample in this experiment.**

A. **In this exploratory experiment, yes.**
Q. **And based on this work on December 18th, Dr. Klingenberg, you decided that the 80 percent full method, if I can refer to it as that, was the one that you were going to use?**
A. **I disagree with that. You go to the next -- to continue in going through the notebook.**
Q. **So you disagree. That's fine.**
A. **Yes.**
Q. **Thank you. The results that you reported in your expert report and testifying about this morning were based on shaking for shear viscosity, were based on shaking on a 80 percent full Erlenmeyer flask?**
A. **That's correct, shaking 80 percent full.**
Q. **And so that, that is the capacity of the flask that you used for the tests that you reported in your expert report and here in court and wanted the Court to rely on?**
A. **Eighty percent full, yes, for shear viscosity.**
Q. **Now, did you ever test the shear viscosity of Nasacort AQ?**
A. **No, I did not.**
Q. **You know that the Kim patents sets out the exact formulation for Nasacort AQ, do you not?**
A. **I do.**
Q. **And you also recognize that the Kim patents, patents**

in suit, state that the recommended shear viscosity for the preferred compounds, compositions in the patent is about 50 to about 200 centipoise?

A. **Yes.**

Q. **And so you agree that testing Nasacort AQ would have provided a good control to be sure that your method, your 80 percent full method actually gave the results stated in the patent, wouldn't it have?**

A. **I suppose, yes, that would -- that could have been done. Yes.**

Q. **So you could have tested Nasacort AQ by exactly the same method that you used to produce the test results that you reported here in court this morning but you did not?**

A. **I did not measure the shear viscosity of Nasacort AQ.**

Q. **And you know that all you had to do was simply ask counsel for Barr for samples of Nasacort AQ and they would have given them to you?**

A. **Sure. I don't think that was necessary here.**

MR. BERGHOFF: No further questions.

THE COURT: All right Mr. Berghoff.

Redirect.

MS. RURKA: Could you please pull up DX-23 at Page 97.

REDIRECT EXAMINATION

BY MS. RURKA:

Q. **Dr. Klingenberg, this is the lab notebook we discussed earlier and you were asked about on cross-examination?**

A. **That's correct.**

Q. **You were asked about the testing of the recovery of Nasacort AQ over five days -- Correct? -- on cross-examination.**

A. **That is correct.**

Q. **And I think counsel asked you to confirm that this testing was done at six RPMs rather than 30 RPMs?**

A. **That is correct.**

Q. **Would that make any difference to your analysis of whether or not this shows that Nasacort AQ takes five days, at least five days to recover its setting viscosity?**

A. **No, I think that the recovery time to get to the setting viscosity will be largely independent of the rotation rate that you use in this viscometer.**

Q. **I'm also going to put up on the Elmo, this is Plaintiffs' Trial Exhibit 1057 which we just looked at earlier?**

A. **Yes.**

Q. **And when you performed or when you created this protocol, you did not know, you had not conducted any viscosity testing on Flonase. Correct?**

A. **I had not conducted any testing on any nasal formulation.**

Q. **Did you know how to conduct the shear viscosity measurements when you created this protocol?**
A. **No, I didn't. It wasn't described in the patents.**
Q. **Is there anywhere in the protocol that tells you that?**
A. **Excuse me?**
Q. **Is there any protocol that says that you didn't know how to conduct the shear viscosity?**
A. **Why, right here in the protocol, item three, it says it's not clear which Burrell wrist action shaker is employed, which position on the shaker, what container volume should be, how full the container is when it's shaken. None of this was specified in the patent so I had to do exploratory experiments trying to figure that out.**
Q. **What did you mean by what container volume is employed?**
A. **It wasn't clear what container or what volume container, should it be a beaker, should it be an Erlenmeyer flask, what it should be and what the volume of that should be or how full that thing should be, full of material.**
Q. **Okay. And that is the last part, how full the container is when shaken?**
A. **That's right.**

MS. RURKA: Would you please pull up Plaintiffs' Exhibit 447?

BY MS. RURKA:

Q. **And I think counsel asked you on cross-examination about this page of your lab notes. Is that correct?**

A. **That's correct.**

MS. RURKA: And the bottom measurement for shear viscosity, could you pull that up?

BY MS. RURKA:

Q. **I think you testified that that matches, the 366 centipoise you measured when you first did -- you did your first measurement for shear viscosity matched up with Dr. Lochhead's results on Flonase?**

A. **That is no longer Flonase at that point. But ...**

Q. **What is it?**

A. **It's Flonase plus air, foam.**

Q. **Is that an accurate shear viscosity measurement of Flonase?**

A. **No.**

Q. **If you could pull to Page 3, please.**

You were also asked about these experiments. There is three here and there is one on the next page. Were these flasks full when you shook them?

A. **Yes. They were full with the exception of the little bit of foam that was at the top of the flask.**

Q. **I believe you testified that these also matched up with Dr. Lockhead's data. Is that right?**

A. **I believe these viscosities, which I would say are not**

shear viscosities, matched, were of similar magnitude to Dr. Lockhead's.

Q. **Were these samples sufficiently deformed, in your opinion?**

A. **No. I don't think this follows the protocol, what there is of a protocol in the patent. These are not deformed significantly.**

Q. **Actually, you were the one who originally said deformed. What did you mean by deformed?**

A. **Deformed, I mean shaken, shared within the flask.**

Q. **Is this like the ketchup example where if the bottle is too full you can't get it shaken up enough?**

A. **Yes, it is. That's right.**

Q. **And then if you could turn to Page 6, what were you attempting to do with these experiments that you discussed with counsel?**

A. **I was attempting to determine how, for various percentages of full, how did those different samples deform if shaken and how much foam is created. Are you creating too much foam while you are trying to deform these samples?**

Q. **So was this the actual shear viscosity measurements you were taking here?**

A. **No. These are still exploratory measurements. I am still trying to figure out how this material behaves at this point.**

MS. RURKA: Thank you. Nothing further.

THE COURT: Thank you, Doctor.

(Witness excused.)

MR. HURST: Our next witness, Your Honor, will be Harry Boghigian, and Renee Sotos from our office is going to handle the examination.

THE COURT: Okay.

MS. SOTO: Your Honor, we would like to call Mr. Harry Boghigian.

... HARRY CHARLES BOGHIGIAN, having been duly sworn as a witness, was examined and testified as. follows ...

THE WITNESS: Your Honor.

THE COURT: Good morning.

THE WITNESS: Good morning.

MS. SOTO: May I approach, Your Honor?

THE COURT: You may.

DIRECT EXAMINATION

BY MS. SOTO:

Q. **Good morning, Mr. Boghigian.**

A. **Good morning.**

Q. **Will you please state your full name for the record?**

A. **My name is Harry Charles Boghigian.**

Q. **Have you come to Court today to testify about your opinion as to whether Nasacort AQ is a commercial success?**

A. **Yes.**

Q. **What qualifies you to give an opinion on that issue in this case today?**

A. **Well, I spent over 35 years in the marketing and commercialization of pharmaceutical products. So I think I am well-equipped to speak on the subject.**

Q. **Can you briefly describe your experience in the pharmaceutical industry?**

A. **Certainly. Be happy to. I started my career with Hoffman-La Roche as a sales representative in 1971, and had the good fortune of receiving a number of promotions over that period of time with increasing responsibilities, that led to a number of senior as well as executive management positions.**

For example, I was appointed to head up all of U.S. marketing for Hoffman-La Roche. I had a portfolio of products on an annual basis that generated 2.3 billion dollars worth of sales in the United States. I had a promotional budget on an annual basis that exceeded 350 million dollars. I had multiple people reporting to me, multiple departments, I should say, reporting to me.

I had a staff of over 270 people.

And, in addition to that, I also was appointed to work with the restructuring of the entire U.S. organization. We turned it into 20 decentralized business

units, with profit-and-loss responsibilities, as well as advertising and marketing responsibilities on a more decentralized basis.

I was appointed senior vice president and general manager for our Canadian operation for Roche Canada. I had the responsibility for revitalizing that organization, turning products around, launching additional new products.

My last position at Hoffman-La Roche was as operations vice president, where I had responsibility with one other colleague for the entire day-to-day operations, profit-and-loss responsibility, and pretty much seeing the continuous success of the organization.

Now, over that entire 30 years of experience with Hoffman-La Roche, I had experiences and disciplines that included licensing, strategic planning, portfolio planning, developed a brand management plan, marketing plans, co-promotion agreements, co-marketing agreements.

I really covered all of the facets and parameters involved in the commercialization and marketing of pharmaceutical products.

Q. **Okay. How many pharmaceutical products did you market and commercialize while you were at Hoffman-La Roche?**

A. **I had experience with over 40 products during that 30-year stint.**

Q. **Is Hoffman-La Roche considered a generic company?**

A. **No. Hoffman-La Roche is one of the top ten research and development companies, brand companies, in the world.**

Q. **What did you do after you left Hoffman-La Roche?**

A. **I left Hoffman-La Roche in June of 2001, and I started in the fall of that year my own consulting company, called Pharma Consultants, which exists today.**

I consult with small- to medium-sized pharmaceutical companies on strategic issues, developmental issues, licensing issues, as well as health care agencies that are looking to work with pharmaceutical companies.

In addition to that, in 2003, I started my own, with two other colleagues, actually, research and development company called PBN Pharma, which is headquartered in Chicago. We have currently 12 patents that we have in different therapeutic areas.

Q. **Okay. And have you been retained in other cases as an expert witness on the issue of whether a pharmaceutical product is a commercial success?**

A. **Yes, I have.**

Q. **About how many times?**

A. **Seven or eight times.**

Q. **Did you testify as to the issue of commercial success in any of those cases?**

A. **Yes, I believe three or four times.**

Q. **Do you consider yourself an expert in the marketing**

and commercialization of pharmaceutical drug markets?
A. Yes, I do.
MS. SOTOS: Your Honor, at this time I would like to offer Mr. Boghigian as an expert in pharmaceutical sales and marketing.
MR. NOE: No objections, Your Honor.
THE COURT: Is it Mr. or Dr.?
MS. SOTOS: Mr.
THE COURT: It says Dr. Mr. Okay. He is accepted.
BY MS. SOTOS:
Q. Mr. Boghigian, what is your understanding as to how to evaluate the commercial success of a pharmaceutical product in the context of nonobviousness?
A. Well, it's my understanding when it comes to commercial success that you need to determine if there is a nexus between the sales and the prescriptions of the product and the claimed patented invention. If there is no nexus between the sales and the patented invention and it's really due to some other external stimuli or extraneous factors, then, obviously, there is no nexus.
Q. And what did you conclude with regard to Nasacort AQ?
A. I determined that there was no nexus.
Q. Before we discuss the details of your opinion, can we summarize the types of documents that you reviewed in

forming your opinion?

A. Certainly.

I personally reviewed thousands of pages of documents. And they focus primarily on the commercialization and marketing of the Nasacort franchise. They were marketing plans, they were strategic plans, they were market research documents. They were budgets.

There was just a host of documents that focused on the marketing and commercialization of Nasacort.

Q. Okay. Did you review the report of Aventis's expert, Dr. Gregory Bell?

A. Yes, I did. In fact, my report is really a rebuttal to Dr. Gregory Bell.

Q. Let's now turn to your opinion about Nasacort AQ. Can you briefly summarize the reasons that you concluded that Nasacort AQ sales are not due to the claimed invention?

A. Yes. In reviewing those numerous documents, it became obvious that, first of all, there was a substantial under-performance of Nasacort AQ versus the competition. In addition, it was very clear that the product was undifferentiated, that Aventis was not able to differentiate the product in the marketplace.

Also, that the sales were really due to advertising and promotion and really due to the fact that this was just triamcinolone acetonide.

Last but not least, there was no evidence that appeared to indicate that this product was profitable on a cumulative basis.

Those were basically the four reasons that I found brought me to my conclusion.

Q. **Let's first talk about the reason that Nasacort AQ under-performed compared to the competition. Against what products did you compare the performance of Nasacort AQ?**

A. **Well, I looked at the entire intranasal steroid market, the products in that particular class. They were the same products that Aventis looked at. I focused in on the products that were the dominant products, which again were the products that Aventis focused on, which were basically Flonase and Nasonex.**

Q. **What measure of performance did you look at to compare Nasacort AQ's performance to those?**

A. **I focused primarily on prescriptions, on dollars, and the market share of prescriptions and dollars in that therapeutic area.**

Q. **Why don't we first talk about prescriptions. How did Nasacort AQ compare to Flonase and Nasonex in terms of total prescriptions?**

A. **There was no question that Flonase and Nasonex were dominant in the class, and that Nasacort AQ trailed in comparison. In fact, Flonase was, in several years, three**

prescriptions to every one of Nasacort AQ, and Nasonex had very similar results of two to one.

Q. Okay. Did you prepare a chart showing this prescriptions analysis that you did?

A. Yes, I did.

MS. SOTOS: Mr. Young, could you please put up Demonstrative 74.

BY MS. SOTOS:

Q. Mr. Boghigian, is this the chart you prepared?

A. Yes, it is a chart of total prescriptions.

Q. And can you please explain what each color represents?

A. Certainly. This again includes new and refills for total prescriptions for each of the three products. Flonase in green, Nasacort AQ in the red and Nasonex in the yellow.

Q. And how does this chart inform your view that the claimed invention did not leave the Nasacort AQ prescriptions?

A. Well, I think it's pretty obvious. You can see there is significant growth. You can see that Flonase had a very steep incline, just continued to grow year after year after year. Nasonex was also introduced after Nasacort and you can see in the yellow that it indeed paralleled Flonase 's growth curve in terms of total prescriptions and both products literally were dominant in the class and Nasacort AQ ended up trailing considerably. It launched in 1996 as

you can see in the red. It had a very short shallow growth curve and then levelled off in 2002-2003 and then began to decline.

Q. All right. You just mentioned that Nasacort AQ launched in 1996, but your chart starts in 1994. Can you explain why you started in 1994?

A. Well, the pharmaceutical industry, it's extremely important to look at a product's introduction, the launch phase. It's important because in our industry, physicians will relatively quickly establish a perception of a product and a concept and they'll cement that perception of the product. So I like to look at the product to see exactly what the adoption rate was, what the uptake was with physicians and see how rapid and steep the growth curves are.

Q. Okay. And so what product are we looking at from 1994?

A. Well, in 1994, the data indicates that Flonase was approved in December but for all practical purposes, prescriptions were captured in 1995. And you can see that in their first year they exceed the 2 million total prescriptions.

Q. And you, as a pharmaceutical executive, that has been in the industry for 35 years, how do you evaluate that performance?

A. **I think that is tremendous. That is just a rocket performance. And that's the type of performance you want to see when launch a product: very steep growth curves, very quick acceleration of a product. It indicates great satisfaction with physicians and certainly adoption and uptake.**

Q. **And how does Nasacort AQ compare?**

A. **It trails. You can see very significantly the product was introduced in 1996, was a very shallow uptake, and then quickly leveled off. It was really, really flat. It really trails Flonase and Nasonex.**

Q. **And did you look at the cumulative total prescriptions of these products over the course of their lifecycles?**

A. **Yes, I did.**

Q. **Did you also prepare a chart with that information?**

A. **Yes, I did.**

MS. SOTOS: Mr. Young, can you please put up Demonstrative 73?

BY MS. SOTOS:

Q. **Mr. Boghigian, is this the chart that you prepared?**

A. **Yes.**

Q. **Okay. And how does this chart inform your view that Nasacort AQ prescriptions did not stem from the claimed invention?**

A. **I think it's pretty on use when you look at this. You**

can see Flonase is 17.8 million prescriptions. This is cumulative from 1994-2007. This is the time frame. Those three products were introduced into the market and actually goes to July of 2007. That's the date, the last month that I had IMS prescription data for. And you can see very clearly Flonase accumulated over that period of time dispensed a total of 117.8 million prescriptions, three to one, four to one. You can see with Nasonex again a very similar performance, two to one in terms of prescriptions. I mean it literally dwarves Nasacort AQ.

Q. **And you have been sitting in this courtroom from the beginning of the trial. Is that right?**

A. **That's right.**

Q. **And you heard some testimony that Nasacort AQ is preferred two to one over Flonase?**

A. **Well, that's what I heard. And that was certainly promotional messages that Aventis had that indicated that. However, when you look at this, actually in prescriptions it's really the reverse. The opposite. Flonase is really preferred two or even three to one versus Nasacort.**

Q. **Mr. Boghigian, why don't we turn to the dollar sales comparison you did. How did Nasacort AQ compare to Flonase an Nasacort in that regard?**

A. **It parallels the prescription data we just reviewed. And then you will see very similar trends and patterns as it**

relates to dollar sales of Flonase, Nasonex and Nasacort AQ.
Q. Did you prepare a chart comparing those trends and patterns?
A. Yes, I did.
MS. SOTOS: Mr. Young, can you please put up Demonstrative Exhibit 75.
BY MS. SOTOS:
Q. Mr. Boghigian, is this the chart that you prepared?
A. Yes.
Q. And how does this dollar sales data inform your view that the Nasacort AQ sales are not tied to the claimed invention?
A. Well, again, you can see that the competitors grew very, very quickly. You can see from 1995 through the period 2005 that there was significant growth with Flonase, paralleled with Nasonex, and again Nasacort AQ is trailing behind in terms of dollar sales.
Q. And, again, you began this analysis in 1994 as well?
A. Yes. Again, it's important to look, especially in our industry. It's a high risk industry. We are very interested obviously to see how quickly we can capture dollar sales to cover and recoup our cost of investment, our cost of development. We like to do that within the first three-to-five years to break even so it's important to look at dollar sales to see exactly what that trend and that

pattern is going to be and hopefully continue to build on.
Q. In looking at this chart, if you look at Flonase, it's just going, it's rising up and up and up. And then for 2005 to 2006, you see a decrease. Do you, based on your years of experience in the pharmaceutical industry, have an understanding as to why that decrease occurred?
A. Well, it's my understanding and recollection in 2005 the Flonase patent expired. They stopped promotion of the product; and I think that is why you see a big decline in prescriptions in 2006.
MS. SOTOS: And why don't we turn to the market share comparison that you did.
BY MS. SOTOS:
Q. Did you prepare a chart comparing the products market share as well?
A. Yes, I did.
MS. SOTOS: Mr. Young, can you please put up -- I'm sorry. Mr. Young, can you please put up Demonstrative Number 71?
BY MS. SOTOS:
Q. Is this a chart that you prepared, Mr. Boghigian?
A. Yes.
Q. And how did this market share data inform your view that Nasacort AQ's prescriptions were not due to the claimed invention?

A. **Well, again, you can see the significant market share achieved by Flonase, the type of curve that we ideally like to see in the industry: very steep. And by 2005, it captured 45 percent of the market. Similarly, you see with Nasonex a very similar curve. And yet you see with Nasacort AQ, we have a very shallow growth curve leveling off at about 14, I think it's about 14 and-a-half percent market share in 2006.**

Q. **Okay. And did you calculate or assess at all generally what Nasacort AQ's market share was over the course of this life-span?**

A. **It averaged about 10 percent, 10-11 percent. In 2005 actually, if you looked at the two dominant products, Flonase and Nasonex, they actually had over 70 percent, almost 76 percent of the total prescriptions that were written on this particular class. So there is no question they were the two dominant products, the two that physicians wrote the most for.**

Q. **And how would you evaluate general 10-to-11 percent range of prescription market share?**

A. **Well, with the length of time that this product has been on the market and the fact that triamcinolone has been around, had been available as an intranasal corticosteroid, I would classify this as a failure, extremely disappointing.**

Q. **And did Nasacort AQ displace any of the products in**

the INS class? And when I use the term INS class, just to clarify for the record, it's intranasal corticosteroid?

A. Yes. If I recall correctly, Nasacort AQ really displaced its precursor which was Nasacort aerosol. The inhaler form is what it really displaced.

Q. When you say "precursor," do you mean a prior Aventis product?

A. That's correct. Aventis had on the market, and launched in 1991, Nasacort aerosol or inhaler and it's my opinion that they displaced the inhaler form.

Q. What again led you to make that conclusion?

A. I looked at the market share data. I looked at the trends. I looked at obviously the marketing plans and so forth. And it was pretty obvious that that is what transpired.

Q. And did you prepare a chart showing those market share trends?

A. Yes, I did.

MS. SOTOS: Mr. Young, can you please put up Demonstrative No. 8?

BY MS. SOTOS:

Q. Mr. Boghigian, is this the chart that you prepared?

A. Yes, this is the chart I prepared.

Q. Is that -- what is the blue?

A. The blue is the Nasacort inhaler, which is the aerosol

form.

Q. And is that the claimed invention in this case?

A. I'm sorry.

Q. Is that the claimed invention in this case?

A. No, it's not.

Q. And red, that is Nasacort AQ?

A. That is correct.

Q. And that is the claimed invention?

A. Yes.

Q. And what does this chart tell you about whether there is a nexus between the Nasacort AQ sales and the patented invention?

A. It tells me there is really no nexus. In fact, what it really portrays, they're interchangeable to a great extent. I mean this is a relative -- the scale is only to 18 percent. It pretty much shows that the inhaler form Nasacort AQ peaked at about 16-percent market share in 1994, only about two to three years after it was introduced and then declined. And from what you can see there, as the aqueous form was introduced, it really captured a significant share of the aerosol business as it declined. And then it peaked at about 14 and-a-half percent market share, never even meeting or exceeding the previous market share of the aerosol form.

Q. Okay. And it looks from your chart that the Nasacort

AQ begins to decline in 2004. Do you have an opinion as to why that occurred?

A. **Yes. If you look at the environment at that time, the FDA had mandated that by July of 2003, all aerosol forms that had chlorofluorocarbons as the aerosol delivery system had to be removed from the marketplace. I think it was referred to here earlier this week in the courtroom.**

From the Aventis documents that I reviewed, there was a strategy and a tactic to move that franchise to the aqueous form. And I believe what you are seeing from 2003 to 2004, that increase is the switching of the aerosol business to aqueous business.

And then what happened is after all that transpired and there was no more aerosol to transfer, what you see happening is the continuation of the market environment, the competitive products continuing to grow at the expense of Nasacort AQ. And that is why you see the decline.

Q. **You mentioned some discussion about this switching from the inhaler in the Aventis documents, and I'd like to take a look at some of those documents.**

A. **Certainly.**

MS. SOTOS: Mr. Young, would you please put up Defendant's Exhibit 246?

BY MS. SOTOS:

Q. **Okay. Mr. Boghigian, do you recognize this document?**

A. **Yes.**

Q. **And what is this document?**

A. **This is a document that was created for delivery to pharmacists. As you can see, it says "dear pharmacist" and it identifies Nasacort nasal inhaler at the top and Nasacort nasal spray, the AQ form.**

And if you go down to the second paragraph where it starts with: If a patient presents a prescription for Nasacort nasal inhaler (or asking for a refill) on or after July 24th, 2003, we ask that you assist the patient in the following ways:

Inform the patient that Nasacort nasal inhaler is no longer available.

Inform the patient of Nasacort AQ and the potential for different insurance coverage.

What they're asking the pharmacist to do is assist them in moving the franchise to move from the inhaler form to the aqueous form. And, frankly, it makes good business sense. Since you no longer can market the inhaler form, it makes good business sense as a strategy to try to move that franchise over to the aqueous form; and that's what they did.

MS. SOTOS: All right. Why don't we look at another document. Mr. Young, can you please put up

Defendant's Exhibit 247?

BY MS. SOTOS:

Q. **Mr. Boghigian, do you recognize this document?**

A. **Yes. This is another document that was created. And I believe this one was directed to physicians. And you can see right at the very, very top, it says: Switch your patients to Nasacort AQ -- which is the aqueous form.**

And then further down, I think several paragraphs down, it states: All you have to do is switch them to Nasacort AQ. It contains the same active medication as Nasacort nasal inhaler, in an aqueous formulation. And it provides the same fast, effective relieve from seasonal, and perennial allergies.

So, again, this was a communication, a strategy to assist physicians in transferring the business.

Q. **Okay. We just looked at documents directed to pharmacists and physicians. Were there any documents directed from Aventis to consumers about switching from the inhaler to the AQ?**

A. **Yes, there were.**

MS. SOTOS: Mr. Young, can you put up DX-328, please?

BY MS. SOTOS:

Q. **Do you recognize this document, Mr. Boghigian?**

A. **Yes.**

Q. **What is this document?**

A. **Well, this was a document that was designed to incentivize consumers or patients of record actually who were on Nasacort inhaler. And they were going to incentivize them by encouraging them to go and switch their prescription to the aqueous. As you can see, it says in the bottom left, which is blown up here on the screen:**

Get the same relief from Nasacort AQ.

If you having using Nasacort nasal inhaler, you can get the same relief with Nasacort AQ. It contains the same active medication, triamcinolone acetonide, the same dose per spray, and the same once-a-day dosing. The only difference is the medication is delivered by a water-based formula instead of aerosol.

Again, save up to $15 worth of triamcinolone.

So again trying to incentivize the consumer or the patient to request prescription for the AQ and they'll discount it by $15.

Q. **And did you consider the Nasacort nasal inhalers' market share in the INS market prior to its removal from the market?**

A. **Yes, I did. I looked at the performance of the aerosol as well.**

Q. **Did you prepare a demonstrative showing that comparison?**

A. **Yes, I did.**

Q. **Why don't we take a look at that.**

Mr. Young, can you put up Demonstrative No. 72.

Mr. Boghigian, is this the demonstrative that you prepared?

A. **Yes, it is.**

Q. **How does this support your conclusion that there is no nexus between the claimed convention and the Nasacort AQ sales?**

A. **Basically, this is the positions for the different time frames. They are pretty much the same. Nasacort inhaler, which is in the left-hand graph, you can see is in the dark blue, it's the time frame '92 that goes through 2005. You can see that it was No. 3.**

At that time, Beconase AQ and Vancenase AQ were the two dominant products in the class. They controlled about 66 percent of the market.

So Nasacort AQ in positioning was No. 3.

If we move over to the slide we just saw earlier, which was duplicated here, you can see again, with Flonase and Nasonex entering into the market in '94 and '96, they not only captured a significant share or greater share of prescriptions, but they expanded the market as well. There were many more prescriptions during this period of time. Flonase really drove that market, as even identified

in the Aventis documents.

Again, Nasacort AQ is No. 3. The positioning is saying they are really interchangeable in terms of products.

Q. Given your conclusion that Nasacort AQ cannibalized the Nasacort nasal inhaler, in your view is there a nexus between the Nasacort AQ sales and the claimed invention?

A. No.

Q. Let's move on. You mentioned that you looked at profitability. Why was profitability a factor in your analysis?

A. Well, profitability is important. As I mentioned earlier, I mean, our industry is a very high-risk industry. We have significant cost of capital. We need to be able to recoup our investments relatively quickly. Three to five years is kind of the break-even point we look for.

We need to cover the cost of failures. Again, as a high-risk industry, we have a lot of failures. And the cost, based on a number of sources, indicates that the cost to bring a product to market now runs about 800 million to 1.7 billion dollars.

So as a result of that, there is significant need to recoup that investment, to be able to support the infrastructure of the organization, and to continue to re-invest in additional new product innovations.

Q. Is the timing of when the recoupment of the investment

takes place important to you?
A. Absolutely. I mean, I think that's probably one of the most important elements to look at.
Q. And in your opinion, has Nasacort AQ been cumulatively profitable?
A. No, in my opinion, it has not been cumulatively profitable.
Q. Why did you conclude that it had not been profitable?
A. Well, I looked at, there was one financial document that showed some what was listed as product contribution. It was in the fifth year after introduction of Nasacort AQ. It was only, I believe, 18 million dollars, which a product that's been on the market, being heavily invested in, for five years, four or five years, with a reported product contribution of 18 million dollars, in my opinion, indicates that previous to that you have really been losing money.
Q. And, Mr. Boghigian, I believe we have that document here.
Mr. Young, can you please put up DX-102. Is this the document you were just referencing?
A. Yes. This document actually goes from the year 2000 in actual sales to 2006 in actual sales, and 2007 is a budget number. But this is the first four years of that document. You can see sales at the top, and these are aerosol sales and inhaler sales, net sales. You can see the

reductions that were taken. And then you can see the marketing costs beginning in 2000 at 106 million dollars. Then when you deduct the 106, the 152, and the 139, et cetera, you can see the product contribution at the bottom.

Product contribution in our industry is sometimes synonymous with profit, net profit. Again, this is before GS&A, before taxes, et cetera.

Q. I think you pointed out that this data begins in the year 2000, but Nasacort AQ launched in 1996?

A. Exactly. It launched in 1996, there would have been marketing expenses, launch expenses, for not only 1996, the year of introduction, but obviously for the subsequent years. Looking at this, since there were no other documents, my conclusion is this product has not been profitable on a cumulative basis.

Q. Mr. Boghigian, it looks like the product contribution number actually begins to increase. Doesn't that mean that Nasacort AQ starts to get profitable?

A. Well, it does start to generate some profitability. But there is also, as you can see in the marketing line, a decrease in terms of expenditures. You can see a leveling off of the sales. They are not growing to any significant extent.

It is my feeling what management began to realize at this point, after having a product on the market

since 1996, and if you even go back to the aerosol in 1991, that they weren't going to be able to drive this market without expending additional money, and started to cut back on the financial support resources for it.

Q. Do you think there might have been anything else that caused that increase as well?

A. Well, it's also true, when you look at the pricing, that, indeed, they were increasing price, also, which I think contributed to the net sales line as well over this period of time, actually increasing the price of the product.

Q. An increase in the price of the product and increase in sales?

A. Sales, absolutely.

Q. You mentioned that another reason that you concluded that Nasacort AQ is not a commercial success is that it was undifferentiated.

A. Correct.

Q. Can you please explain for the Court what you mean by the term undifferentiated?

A. Undifferentiated in our industry means really the products in that competitive search is very interchangeable. It's almost like a "me, too" product. There is nothing that distinguishes the product and any of its attributes from any of its competitive products. There is no ability to

differentiate, no ability to identify or distinguish any characteristics.

Q. **Do pharmaceutical companies generally want to differentiate their products?**

A. **Certainly. Every good product director, brand manager, that is the first thing he looks for, is how can I differentiate this product. How can I identify a value proposition? In other words, what can I offer the physician and consumer that's superior? Whether it be clinical outcome, safety, whatever. How can I give them something to help differentiate something from the competition.**

Q. **And did Aventis differentiate Nasacort AQ?**

A. **They tried. I give them credit. They had multiple marketing messages that attempted to differentiate the product from the competition. In my opinion, I think they failed in their attempt to do that.**

Q. **Mr. Boghigian, you mentioned the term marketing messages. Can you just explain what that means?**

A. **Well, in our industry, obviously, our marketing people, brand managers, will identify messages that they will communicate to physicians as part of their visitations to physicians, as well as the same messages go into the advertising piece, and if you are going direct to consumers the same thing, so that you have continuity. That the personality of the product is the same.**

When I looked at the Aventis documents, they had multiple messages. And they kept changing those messages as well.

Q. **Well, we will get to the messages in a minute. You mentioned that they kept changing the methods. What does that indicate to you as a pharmaceutical executive in marketing?**

A. **It was my opinion in reviewing those documents that they were struggling. They couldn't find the particular message that they could hold onto that would appear to motivate physicians to use Nasacort AQ versus the competition.**

So they kept trying, in my opinion, different types of messages to try and do that.

Q. **What were some of those messages?**

A. **Well, they had the umbrella message, which was a choice message. You know, we have the aerosol, which is the dry formulation, we have the wet formulation, which is the aqueous, so we can allow the consumer or the physician to choose one formulation versus the other.**

They had this Nasal comfort campaign that they had for a period of time.

They had first-day relief, was another message they tried to communicate.

They had the patient preference message

indicating that patients preferred their product. In addition to that, they had taste-free and odorless, was a message that was intertwined over the years. They also had stays or it sprays, was a message that was communicated very frequently as well.

Q. **These are some of the messages that you saw in the many Aventis documents that you reviewed?**

A. **I am sorry?**

Q. **These are some of the messages that you saw?**

A. **Correct. There were many, many messages that they created and developed.**

Q. **In all of the Aventis documents that you reviewed, did you see any evidence at all that Aventis marketed Nasacort AQ on the basis that it deposits on the frontal sinus?**

A. **No, I didn't.**

Q. **Did you see any evidence at all that Nasacort AQ marketed -- Aventis marketed Nasacort AQ on the basis that Nasacort AQ treats infections in the frontal sinus?**

A. **Absolutely not. I didn't see anything like that.**

Q. **I would like to take a look at some of those documents that you considered. Why don't we put up Defendants' Exhibit 334.**

Mr. Boghigian, what is this document?

A. **This is actually an Aventis sales training document from their sales training group. And it is a document that**

was used or outlined the training for new representatives, as well as in my opinion for existing reserves on how to sell Nasacort.

Q. Is this a document that you considered in forming your opinion?

A. Yes.

BY MS. SOTOS:

Q. Mr. Boghigian, are these just some of the messages that you were talking about earlier?

A. These are some of the messages I mentioned. And obviously there are additional messages here which I didn't mention that they used.

MS. SOTOS: Mr. Young, can you go to Page 29, please?

BY MS. SOTOS:

Q. And, Mr. Boghigian, how does this page inform your view there is no connection between the Nasacort AQ sales and the patented invention?

A. I mean, they basically identified that physicians see them all the same, these products are all the same and that Nasacort AQ is really no different than any other products.

Q. Did you see any discussion in the Aventis documents about a particular term that was used to describe the INS product class?

A. Yes. In fact, in their own documents they identified

these as really commodity market, commodity products. That indeed they could be switched from one product to another. That they're all the same. In several of the documents, they identified this whole market including Nasacort as a commodity market because they couldn't be differentiated.

MS. SOTOS: Let's look at another document. Can you put up DX-120, Mr. Young?

BY MS. SOTOS:

Q. Mr. Boghigian, is this the document that you considered?

A. Yes.

Q. And what is this document?

A. Well, this is a document from Steve Talbert.

Q. And who is Steve Talbert?

A. Steve Talbert is the senior analyst in market research for Aventis. He was assigned to the Nasacort team. And he is basically questioning, as you can see, and this is -- by the way, this is April 5th, 2004.

Q. So that is how many years after Nasacort was launched?

A. Nasacort AQ launched in 1996, so you have almost eight years here in terms of the span. And you can see that in the bulleted point, the paragraph that we have highlighted, he is basically saying: I question this patient preference direction. You know, is this compelling enough to change prescribing habits? The preference issue has existed for

some time, and this is not exactly certain exactly how long. And if it's not driving us in the right direction, then perhaps it's time to try another.

HFA could become a compelling differentiation feature and thus message. "Doc, now you have a choice."

He is referring to HFA which is the new aerosol form that was to replace Nasacort aerosol. In other words, we took out the chlorofluorocarbons. And instead of CFCs, it was going to be HFA was going to be the new aerosol in the new dry form they were going to introduce. He was basically saying maybe that will help us differentiate the product.

He goes on to say in a paragraph further on in this document that, sure, there is going to be some cannibalization from Nasacort AQ. He is not sure what the financial implications are going to be due to cost of goods. But this is a formulation that can help us take from our competitors that we have not been proven able to do what the status quo. In other words, this may help us do what we have not been able to do what to date, and that is capture market share from our competitors.

Q. In fact, you mentioned this document was drafted in 2004. Right?

A. That's correct.

Q. When we were looking before at your analysis of the

market share of the inhaler versus the Nasacort AQ, you described in 2004 something began to happen to the share of the Nasacort AQ?

A. The Nasacort AQ peaked at that point, 2004 as a result of moving the aerosol over.

Q. And then?

A. And then began to decline. Market forces, competitive forces caused the product to decline. I think in 2005, it ended up at 10.3 or 11 percent, somewhere in that ballpark.

Q. So what is Mr. Talbert, the senior analyst, of marketing research at Aventis Pharmaceuticals. What does this e-mail say to you as a pharmaceutical marketing executive Aventis's ability to differentiate Nasacort AQ?

A. He is saying we've not been successful doing that and that, hopefully, this other formulation will help.

Q. We spoke earlier about your conclusion there was switching from the Nasacort nasal inhaler and to the Nasacort AQ and that was responsible for sales of Nasacort AQ. Is there anything else that was responsible for Nasacort AQ sales?

A. Well, I think it's certainly the advertising and promotion was a big factor and the fact that it's triamcinolone acetonide. I mean it's really the same steroid just in another formulation. So I think those are really some of the reasons why.

Q. **Okay. We talked about that, the steroid impact. Why don't we talk a little bit about the marketing promotion that you just mentioned.**

What led you to conclusion that the level of marketing and promotion that Aventis put behind Nasacort AQ was a reason for its sales?

A. **Well, when you looked at that chart, that financial statement from earlier, when you looked at that from 2000-2007, they were spending over 50 percent of net sales to attempt to generate the top line.**

MS. SOTOS: All right. Why don't we take another look at that document. Mr. Young, could you please put up DX-102?

BY MS. SOTOS:

Q. **And, Mr. Boghigian, did you attempt to calculate -- I think you mentioned about 50 percent. So you attempted to calculate the amount that Aventis spent on marketing and promotion. Is that right?**

A. **That's correct.**

Q. **Okay. And can you run us through that calculation?**

A. **Certainly. I took the actual sales which are net sales for the period 2000 through to 2007, recognizing that that was a budget number, $296. And then I added that up and I believe it comes out to $1 billion, 899 million dollars. Then I took the marketing line and added that up**

and it comes to almost a billion dollars, I think $966 million. And when you look at that, I mean here is a product that was introduced in 1996. And yet for the period 2000 and 2006, you have a percentage of over 50 percent of your net sales being committed to continuing to try and drive the product without any real significant uptake in terms of sales. If you look at the years 2005-2006, they're flat at $266 million and yet you are spending $114 million in one year and $87 million in another year. You are not getting any movement on the sales.

Q. Did you try to calculate Aventis's return on its Nasacort AQ marketing expenditures?

A. I did. I looked at actual sales and then I looked the actual marketing and I did a ratio. It ranged anywhere from I think it was a dollar twenty-four was the return in sales for every dollar of marketing that was consumed to I believe it was a high of three dollars and five cents as a range.

Q. And did you use this document to calculate that ratio?

A. I used that document. And if you average it, it was about a dollar ninety-four in terms of net sales for every dollar spent, which frankly is not very good. I would consider that to be extremely high in terms of a cost of marketing.

Q. Okay. And this is an Aventis document?

A. That's correct.

Q. **And did Dr. Bell attempt to calculate the amount of promotional dollars Aventis spent on Nasacort AQ?**

A. **Yes, he did.**

Q. **Did he attempt to calculate a return on the promotional dollars Aventis spent on Nasacort AQ?**

A. **Yes, he did.**

Q. **And what was his result?**

A. **Well, Dr. Bell had a result of $5.55 on everything for every dollar marketing that was spent.**

Q. **Mr. Boghigian, that sounds quite a bit different from the numbers that you just described. Why?**

A. **Well, Dr. Bell used the industry number from IMS, which is an estimate. IMS is a company that provides dollar sales. And IMS calculates it on wholesale price. So you have a price in terms of dollars of sales which is 16 to 20 percent higher than the wholesale acquisition price, so you have an inflated dollar sale number. Then he also used the IMS numbers from the promotional audits which we know in the industry is understated. So when you have inflated sales number and understated expense number and you do the ratio, the calculation, you are providing one into the other, you come up with a much higher ratio and that is how he achieved a $5.55 average.**

Q. **Did Dr. Bell have access to this document, DX-102?**

A. **Yes. Yes, he did.**

Q. **Can you think of any reason why Dr. Bell did not in his report calculate Aventis's return on Nasacort AQ with the numbers in this document rather than IMS data?**

A. **No.**

Q. **Would you, as a pharmaceutical executive that has been in the industry for 35 years, have used the IMS data to calculate that ratio?**

A. **Not for that purpose, no. I wouldn't do it to determine what the ratio is using IMS data. No.**

MS. SOTOS: Okay. That's all I have on direct, Your Honor.

THE COURT: All right. Counsel, about how long do you anticipate your cross will be?

MR. NOE: Perhaps 10-15 minutes.

THE COURT: Okay. Let's do cross. Then we'll do lunch.

MR. NOE: Good morning, Mr. Boghigian.

THE COURT: We'll take lunch after redirect. I'm sorry. We'll let her redirect and then we'll take lunch. Okay. Go ahead.

CROSS-EXAMINATION

BY MR. NOE:

Q. **Good morning, Mr. Boghigian. We have not met. My name is Jeremy Noe, one of the counsel for Sanofi-Aventis in this litigation.**

A. **Nice meeting you.**

Q. **Nice meeting you. Mr. Boghigian, just a few questions.**

First, on the issue of your testimony regarding I believe you referred to it as cannibalization of market share between the Nasacort AQ and the Nasacort inhaler.

MR. NOE: Mr. Young, if you'd could call up DX-8, please?

BY MR. NOE:

Q. **This demonstrative that you have discussed here this morning.**

I apologize. One moment, Your Honor.

THE COURT: Yes.

(Pause.)

MR. NOE: I apologize. This is the wrong demonstrative. I apologize.

THE COURT: No problem.

BY MR. NOE:

Q. **Mr. Boghigian, this chart that you prepared is based on market share, not sales or units. Is that correct?**

A. **That's correct. It's the percent market share of prescriptions.**

Q. **And, in fact, the market was growing, was it not?**

A. **Yes.**

Q. **So, indeed, the growth rate of Nasacort AQ compared to**

what was actually more than twice that of the market. Is that not right?

A. In terms of percentages, it was growing. In absolute numbers, it was significantly trailing the competition.

Q. But the percentage growth weight of Nasacort AQ was more than twice that of the market. Is that right?

A. If I recall correctly, in some of the years it was. I don't believe in every single year.

Q. And with this chart, based on market share, not sales or units, it really doesn't shed much light on the question of whether the decline in units or sales of Nasacort aerosol matched the rise in units or sales terms for the Nasacort AQ. Isn't that right?

A. I'm not sure I understand your question.

Q. This chart that you prepared is based on market share and I believe that you testified that there is virtually a one-to-one correspondence and that Nasacort AQ cannibalized market share from Nasacort aerosol. Is that correct?

A. I believe my statement, my comment was that there was interchange, that there was switching that went on and that there was indeed a significant portion of possibly these patients who went to the AQ form.

Q. You also testified that Flonase and Nasonex were dominant in the marketplace. Is that right?

A. That's correct. In terms of prescriptions and

dollars, yes.
Q. Isn't it true Nasacort and Flonase were spending more on marketing than Nasacort AQ?
A. Well, again, I don't have that. I don't have that data to be able to determine that. All I have is IMS data and that is understated or that's an estimate.
Q. But I believe you testified that it would be understated by about 20 percent. Is that right?
A. No, that's not correct.
Q. How is IMS data understated?
A. I don't know what the percentage of promotional dollars in terms of what that actual percentage is. I know that IMS gathers that from panels of physicians but it's based on the type of input that they get, but indeed when you compare some of the IMS promotional dollars in terms of marketing expenditures to what you see in the actual Aventis marketing, they're significantly understated. In fact, in one year, the Aventis marketing expenditures is $106 million and yet the marketing expenditures of IMS were $40 million so they're not reliable numbers.
Q. But you would agree with me IMS data indicates that Flonase and Nasacort were spending more than Nasacort AQ?
A. It appeared as an order of magnitude that they were probably spending more but I don't have again the actual numbers. That's really what you need to look at.

Q. **On the issue of nexus and your testimony today, that you did not see evidence of sales linked to patented attributes of Nasacort AQ?**

MR. NOE: If I could call up DX-74. I'd like to revisit this exhibit.

BY MR. NOE:

Q. **Mr. Boghigian, are you aware that odorlessness is one of the patented attributes of Nasacort AQ?**

A. **I'm not sure what specifically are in the claimed invention in terms of patented features. I looked at all of the features of Nasacort AQ.**

Q. **You said that you are not sure what the patented attributes of the product at issue in this litigation are?**

A. **Oh, no. I understand that it's thixotropic and it's taste-free, or thixotropic and odorless. I understand that.**

Q. **You agree that odorlessness is one of the patented attributes?**

A. **It is one claimed, I guess, from what I understand.**

Q. **And looking at this demonstrative, are you aware that Nasonex reformulated their product in about the 2004-2005 time frame to eliminate phenyl ethyl alcohol, the rose-scented material?**

A. **Yes, I do recall that.**

Q. **Looking at your own demonstrative here, for the Nasonex sales, which are shown in yellow, from the 2004 time**

frame, there is a rise in prescriptions, is there not?
A. Yes.
Q. Isn't that an indication that there is a demand in the marketplace for an odorless product?
A. No, I don't think you can draw that conclusion from that. There are many other factors that go into marketing in terms of the promotional mix that, indeed, could account for that. Not just that one attribute.
Q. And again, Nasonex was outspending promotionally compared to Nasacort AQ. Is that correct?
A. I don't know that for a fact. I have not seen their actual marketing expenditures from the company. All I have as a guide is the IMS data.
Q. Moving on to DX Demo 75, Mr. Boghigian, this demonstrative that you discussed, we have dollar sales on the y axis. Right?
A. Yes.
Q. Dollar sales are really IMS data, aren't they?
A. That's correct. In this particular slide they are IMS dollars.
Q. Indeed, when you worked at Hoffman-La Roche you used IMS data to track the performance of products. Is that not right?
A. We looked at that as an estimate. Since IMS is a third party audit, an independent audit company, we looked

at IMS data to provide some insight in terms of what the growth curves look like, how quickly the adoption rates were. We looked at that, but we focused more on prescriptions.

Q. Indeed, you used IMS data in preparing your own expert reports submitted in this litigation, did you not?

A. Correct.

Q. And so you consider IMS data for prescription products to be reliable?

A. Yes. I think the industry and my colleagues would agree that there is a degree of reliability with the prescription data.

Q. And that reliability would extend to determining the relative ranking of products in the marketplace. Correct?

A. When you look at prescriptions as it relates to market share, yes.

Q. And relating to your comment a few minutes ago about the understating, I believe you called it, of IMS data, isn't it true that there is no way to determine actual sales data of competitors because companies do not regularly publish that kind of information?

A. That's correct.

Q. So in comparing product sales within a market, isn't IMS data similar audit data? Isn't that the only alternative available?

A. **Dollar sales. If you are looking into a comparison of products, in a particular therapeutic area, then you would look at IMS or Verispan, which were the two major companies. You would look at dollars to get some idea of order of magnitude. But I think most of my colleagues would first look at prescription data, because that's not affected by pricing actions or AWP, et cetera.**

MR. NOE: Thank you, Mr. Boghigian. No further questions.

THE COURT: Any redirect?

REDIRECT EXAMINATION

BY MS. SOTOS:

Q. **Hello again, Mr. Boghigian.**

A. **Hello.**

Q. **Opposing counsel asked you about some numbers, about the growth rate of Nasacort AQ, and asked you about the growth rate of Nasacort AQ being doubled out of the IMS market. Right?**

A. **That's correct.**

Q. **Do you recall that? In your opinion, based on all the analysis you did and your 35 years of experience, was the growth rate of Flonase and Nasonex -- is Flonase and Nasonex growing at a faster rate than Nasacort AQ?**

A. **Yes, it was.**

Q. **He also asked you some questions about Nasonex, and he**

showed you your charts and showed you that Nasonex seemed to increase a little bit in 2004 prescriptions. Is that correct?

A. Correct.

Q. And he asked you if you thought that was due to the fact that they removed the alcohol from Nasonex in 2004? Do you remember that?

A. Yes.

Q. How many -- when did Nasonex launch?

A. I believe they launched in 1996-'97, that time frame.

Q. That is about the same time frame that Nasacort AQ launched. Right?

A. Correct.

Q. So Nasacort AQ didn't have any alcohol from 1996 and still doesn't?

A. Correct.

Q. Nasonex had it from the time that it launched, and yet according to what you said earlier Nasonex was doubling the performance of Nasacort AQ?

A. That's correct.

THE COURT: Are you going to testify, counsel, or are you going to ask a question?

BY MS. SOTOS:

Q. Was Nasonex doubling the performance of Nasacort AQ?

A. Yes. Nasonex was running at a rate in terms of

dollars and prescriptions of two to one.

Q. Why don't we put up -- it's already up there, thank you, Mr. Young.

Opposing counsel asked you some questions about this demonstrative that you prepared. I just want to ask you this question. If you actually had Flonase and Nasonex actual dollar sales data from the companies that own those products, would you have used IMS data to create this comparison?

A. Absolutely not. I would have used the actual data because I can't spend the IMS dollars. I can only spend what I can generate in actual dollars.

MS. SOTOS: Thank you, Mr. Boghigian.

THE COURT: Mr. Boghigian. Thank you, you are excused.

THE WITNESS: Thank you. Pleasure, Your Honor.

THE COURT: We will come back at 1:30.

(Witness excused.)

(Luncheon recess taken.)

THE COURT: All right. Please be seated.

MR. HURST: Your Honor, our next witness is Dr. Thomas Needham.

And while he walks his way up, I would like to officially put into evidence -- I know all the evidence is in -- the interrogatory response confirming Aventis's

reduction to practice, May 1st, 1992, with respect to the public use defense and, in particular, the experimental use exception to inapplicability as Defendant's Exhibit 284. Pages 3 and 4 identified the reduction to practice dates.

THE COURT: I'm assuming there is no objection.

MR. BERGHOFF: I'm simply reserving our objection that was the subject of the motion in limine, Your Honor.

THE COURT: Same ruling.

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DEFENDANT'S TESTIMONY

... DR. THOMAS EDWARD NEEDHAM, having been placed under oath at 1:35 p.m. as a witness, was examined and testified as follows ....

- - -

MR. HURST: Before we get started, may I?

THE COURT: You may.

(Binders passed forward.)

DIRECT EXAMINATION

BY MR. HURST:

Q. Dr. Needham, starting off, how are you currently employed?

A. I'm a Professor of Pharmaceutics in the College of Pharmacy at the University of Rhode Island.

Q. And how long have you been there?

A. **I've been there since 1989.**
Q. **For background purposes, can you explain to Judge Sleet your educational background, please?**
A. **Yes. I have a bachelor's degree in Pharmacy, and I'm a registered pharmacist. I also have two graduate degrees: a master's degree and a Ph.D. in Pharmaceutics.**
Q. **And when did you get each of your degrees?**
A. **The master's in 1967. And the Ph.D. in 1970.**
Q. **From? All from?**
A. **Everything was from the University of Rhode Island.**
Q. **Which is where you are now?**
A. **Yes.**
Q. **So how long have you been in the field of pharmaceutical formulations?**
A. **Since 1970, so almost 40 years.**
Q. **So you got your Ph.D. from the University of Rhode Island in 1970. What did you do then?**
A. **I went to the University of Georgia School of Pharmacy and taught there. The usual: taught classes, set up a research program. What faculty usually do.**
Q. **What kind of professor were you also there?**
A. **I also was a Professor of Pharmaceutics there, too.**
Q. **Generally, what subject matter did you teach?**
A. **Well, to undergraduates, I taught about dosage forms and their characteristics and how they would use them, the**

stability, just the basic knowledge that a pharmacist uses. And to graduate students, it becomes a little more complicated. I taught pharmaceutical formulations, physical pharmacy for regular and drug-delivery-type-based dosage forms. I taught a little bit about manufacturing, regulatory affairs, that type of thing.

Q. So forgive me if you said. 1979 was the year you left the University of Georgia?

A. Correct.

Q. Have you been in academia your entire career?

A. No. I left the University of Georgia as we said in 1979 and went to work for, at the time it was called Baxter Travenol. It's now called Baxter healthcare.

Q. Okay. What did you do at Baxter?

A. I was in their central research area. I was associate director of what they called pharmaceutical development. So basically I had responsibility for product development, formulations, manufacturing, scaleup, interfacing with the manufacturing groups. And then later on, I had more responsibility for like technology, evaluation and searching in the drug delivery area.

Q. And you remained at Baxter until when?

A. I was there until 1986, and then I went to work for Searle Monsanto, mostly in the Searle portion of it in Illinois in their research area.

Q. **Okay. So you stayed at Searle until when?**
A. **1989.**
Q. **What did you do then?**
A. **Then I went back to the University of Rhode Island as faculty member.**
Q. **And are you still at the University of Rhode Island?**
A. **Yes.**
Q. **So how long have you been there? I can probably do the math for you. 20 years?**
A. **Almost 20 years.**
Q. **20 years. And what do you do there? What is your occupation there?**
A. **I'm a Professor of Pharmaceutics. And as to what I do, again I teach undergraduate students about the dosage forms. It's a professional school so you teach the pharmacists, future pharmacists. And we also have a graduate program for master's level and Ph.D. level. And I teach them about formulations, drug delivery, manufacturing, regulatory affairs, that type of thing.**
Q. **Have you held any positions of leadership at the University of Rhode Island?**
A. **Yes. I was Chair of the Department of Pharmaceutics for 12 years. I've since given that up.**
Q. **Have you done research since your time, since you began at the University of Rhode Island?**

A. **Yes. We set up our research, drug delivery research laboratory and we did a lot of work for different companies as well as got grants and such.**

Q. **Do you have any patents?**

A. **I have five patents.**

Q. **Okay. How about publications?**

A. **I have 75 peer-reviewed publications.**

Q. **How many times during your career have you personally, by yourself, actually made a physical pharmaceutical formulation with an active ingredient in it?**

A. **Dozens of times.**

Q. **Yesterday, we heard some testimony suggesting that a pharmaceutical formulator doesn't do this by themselves. It's always a large, large team. Has that been your experience?**

A. **No. Even in industry, ultimately there is one person responsible for the formulations. I mean the product development may have a team with people from different areas but there is a pharmaceutical pharmaceutics guy essentially who has responsible for the formulation.**

Q. **You know this case is about nasal sprays. Right?**

A. **Yes.**

Q. **Have you ever formulated a nasal spray?**

A. **Yes, many of them.**

Q. **Of your 75 articles, how many of your articles relate**

to nasal sprays or nasal products?
A. About 12 or 13 of them.
Q. How about of your five patents? Did any of them relate to nasal sprays?
A. Yes, two are in the area of nasal drug delivery.
Q. Are any universities in the United States considered to be leaders in terms of research and experience with nasal sprays?
A. Yes, there are several. And I'd like to think that the University of Rhode Island is right near the top of that list. Obviously, Dr. Donovan's program at the University of Iowa is there; and the University of Kentucky; maybe University of Missouri, Kansas City. There are five or six groups that do a little bit in the nasal area.
MR. HURST: Your Honor, I'd like to proffer Dr. Needham as an expert in the formulation of pharmaceutical products, including nasal sprays.
MR. BERGHOFF: No objection.
THE COURT: The doctor is accepted as an expert in that area.
THE WITNESS: Thank you.
BY MR. HURST:
Q. Now, doctor, we asked you to conduct an analysis in this case. Correct?
A. Yes.

Q. **What analysis did we ask you to conduct?**
A. **You asked me to look at the patents and to really evaluate if there was a potential for a person of ordinary skill in the art to look at those patents and consider them to be obvious.**
Q. **And for this proceeding, I asked you to focus on Claim 6 of the '573 patent and Claim 26 of the '329 patent. Correct?**
A. **Correct.**
Q. **Do you have an opinion on whether or not those claims in 1996 would have been obvious to one of ordinary skill in the art?**
A. **Yes, I think they are.**
Q. **All right. Do you have -- okay. Let's move on. Claims in this case are aqueous formulations of nasal sprays. Correct?**
A. **Correct.**
Q. **And was Aventis the first to develop an aqueous formulation of a nasal spray?**
A. **No.**
Q. **Before Aventis made any formulation in this case, were other aqueous formulations available?**
A. **Yes, there was Beconase AQ sprays, there was Vancenase AQ sprays and there was a Flonase. All of these were on the market before that '95 time frame.**

Q. **Are all these prior art products?**
A. **Yes.**
Q. **Do these prior art products in your mind in summary support your opinion that the claimed invention is obvious?**
A. **Yes.**
Q. **Did anything prompt the development of aqueous nasal spray formulations as of the 1980s, before Aventis came along with Nasacort AQ?**
A. **Yes. We've heard the talk about the impending CFC ban and the issues around the environment with that. And it was well known that the use of CFCs was going to be banned and withdrawn sooner or later.**
Q. **How did that impact the pharmaceutical industry?**
A. **Well, you have the nasal aerosol products which were propelled by CFCs. So if they were banned, they would have to replace those products.**

MR. HURST: Let me take a look at Defendant's Exhibit 297. Just blow up the first part to identify this.

BY MR. HURST:

Q. **Do you see the date there?**

MR. RICH: Your Honor, if I might object.

THE COURT: Basis.

MR. RICH: This is a document that this expert did not --

THE COURT: Speak up, please.

MR. RICH: I'm sorry. This is a document that this witness did not consider in relation to the formation of his opinions. And we believe it is inappropriate to allow it in with his testimony.

THE COURT: Mr. Hurst, your reaction.

MR. HURST: Yes. This is a document in evidence. I'm not actually going to ask him to do anything.

THE COURT: Did he consider it?

MR. HURST: He did not.

THE COURT: Take it down.

MR. HURST: All right.

THE COURT: Objection sustained.

MR. RICH: Thank you, Your Honor.

BY MR. HURST:

Q. **The CFC ban that you referred to, is that something that was known to those of ordinary skill in the art in the late 1980s?**

A. **Yes. Because of its impending impact, a person of ordinary skill in the art would be well aware of the issues around the ban.**

Q. **Thank you.**

MR. HURST: Why don't we go to Demonstrative Exhibit 29. Defendant's Demonstrative Exhibit 29.

BY MR. HURST:

Q. **So how did the issue with CFCs impact in particular**

nasal spray development? And we prepared a demonstrative exhibit to help us walk through this?

A. **Yes.**

Q. **So can you explain what we're looking at to Judge Sleet, please?**

A. **Well, we're looking at, firstly, the Vancenase CFC-based aerosol. Essentially, what is important is all of these glucocorticosteroids were for the most part originally formulated as aerosols using CFCs to propel them, if you will, or administer them. And you can see that the Vancenase was approved in 1981. And what they did, as part of the impending ban, was to develop a Vancenase AQ suspension which was approved in 1987.**

SmithKline likewise with the same drug, basically had the Beconase CFC, again approved in 1981. That was then switched or reformulated to the Beconase AQ, approved in 1987.

And then Flonase, which is an aqueous suspension, never -- it came out its first time as an aqueous suspension I think because of the fact that they knew of the CFC impending ban and didn't even bother with the aerosol product.

Q. **Okay. So then Aventis comes along later in time, at least with respect to Beconase and Vancenase, and what happened with respect to Aventis?**

A. **Well, Aventis had the Nasacort CFC-based aerosol approved in '91. And they, as I think we can see from some of their documents, realized that they had to switch out of the CFC and reformulate to an aqueous product.**

Q. **Okay. Now, in addition to these prior art products, are you aware of any published patent applications prior to Aventis's work that also referred to this switch from a CFC-based product to an aqueous based nasal spray?**

A. **Yes, there was.**

MR. HURST: Why don't we take a look at Defendant's Exhibit 13. If you can just highlight the top right-hand corner.

BY MR. HURST:

Q. **Can you tell us what we're looking at here?**

A. **Well, you can see this is international patent application that was filed on September 3rd, 1992.**

Q. **Okay. And what does it relate to?**

MR. HURST: It might help if we highlight the abstract.

A. **So you can see it's an aqueous suspension formulation. The active ingredient is the glucocorticosteroid tipredane and it's used for treating allergic, or as it says immune reactions.**

BY MR. HURST:

Q. **Okay. Why don't we take a look at, there is a part in**

here that refers to the issue we were talking about before?
A. Yes.
MR. HURST: It is Page 3, last paragraph.
BY MR. HURST:
Q. What does this relate to?
A. Well, basically they're talking about the fact that the CFC driven formulations are unsatisfactory from an environmental perspective and that the HFC propellants are difficult to formulate. So they're well aware of the fact, the issues around the CFC.
Q. So what did this patent, published patent application say with respect to the solution for avoiding the CFC problem for nasal sprays?
A. Well, essentially they're going to have to develop another drug. They're going to have to stop using the CFCs.
Q. And what in particular does this patent application recommend doing? Or what do they do? What kind of nasal spray did they come up with?
A. They came up with an aqueous suspension.
Q. Now, you reviewed Aventis documents in this case. Correct?
A. Yes.
Q. Development documents and so forth?
A. Correct.
Q. Do you have an understanding of what prompted Aventis

itself to convert from a CFC-based based aerosol to an aqueous-based formulation?

A. Yes, I do.

Q. What is that?

A. Well, basically, they are in the same boat as everybody else. They are seeing the impending need to change. And they are looking at the environmental issues around. I think there is a memo. But basically, they look at the fact they are going to have to look at an aqueous suspension.

Q. Let me take a look at the memo I know you are referring to, Defendant's Exhibit 33. If you can highlight the top there, so we can explain what we are looking at here?

A. Yes. This is an internal interoffice memo from March 1st, 1991, that basically defines their rationale in developing the Nasacort AQ products.

Q. Why don't we -- this is a 1991 memo. You did say that.

-- take the fourth paragraph and blow that one up.

What does this paragraph refer to in terms of explaining why Aventis decided to develop Nasacort AQ?

A. Well, basically they are saying if and when this ban becomes effective, they are going to have to replace the

Nasacort aerosol, is what they are talking about.

The other issue, basically, is the lost business. If an AQ formulation is not developed, they are going to lose about a hundred million in annual sales.

Q. **In your mind, is it innovative thinking as of March of 1991 to convert CFC-based aerosol nasal spray to an aqueous nasal spray?**

A. **Not at all. There are already two products on the market that have done this, the Beconase that I talked and Vancenase, they are the same class of drugs, glutamine corticosteroids. And they were converted successfully and passed all FDA testing and clinical efficacy.**

Q. **Why don't we take a look at the second paragraph. We will take it a line at a time. To what does this first line refer? Does this refer to what we were just talking about?**

A. **Yes. This talks about the current intranasal steroid market is predominantly aqueous. That refers back directly to the two products, the Beconase and the Vancenase AQ that were on the market. And they had 60.7 percent of the share.**

So the other issue that they mention is that physicians currently perceive the aqueous preparations are more comfortable than the aerosols.

Q. **This reference to physicians believing that aqueous preparations are more comfortable, that is an internal Aventis document. Right?**

A. **Yes, it is.**

Q. **Well, are you aware of published prior art that says the same thing?**

A. **Yes. I can think of three articles. There is an Orgel article. Then there is the Setipane and Kobiashi articles that make note of this fact.**

Q. **Why don't we look at the Setipane article. That is Defendant's Exhibit 10. Blow up the top so we can put a date on it.**

A. **So you can see, this is published in Clinical Therapeutics in 1995. It talks about triamcinolone aqueous nasal spray, studies to evaluate in a double-blind study patients with seasonal ragweed, allergic rhinitis.**

Q. **You understand, it is your understanding this is a prior art document?**

A. **Correct.**

Q. **Take a look at Page 1, we will stay in the abstract. Why don't we blow up the first five or six lines of the abstract. I guess the first thing I wanted to ask you about is, is this a published reference talking about that preference that you were discussing?**

A. **Yes. Basically, it says right in the first line, because some patients may prefer aqueous sprays, so it talks about -- then it follows with once-a-day dosing. A new aqueous formation of triamcinolone acetonide TAA aqueous was**

developed.

Q. What drug is this published article about?

A. Nasacort AQ.

Q. The drug that's claimed in the patents at issue?

A. Yes, exactly.

Q. What does this article disclose about Nasacort AQ in the prior art?

A. Basically, it discloses the drug as an aqueous formulation. Also, a person of ordinary skill in the art would know that we are talking about a suspension, because this drug notoriously has a low solubility in water, so the only way to deliver a full dose would be with a suspension product.

We know the vehicle is water. It says right there.

Later it talks about the fact that the product is a thixotropic product.

Q. Does it disclose anything about the dosing for Nasacort AQ?

A. Yes, it also does. It gives the dosing, and shows, because it's a clinical study, shows that it's an effective dosing.

Q. So what's your understanding of Aventis's argument related to why the claimed inventions are sustainable even though the Nasacort AQ is published in the prior art?

A. **Well, I guess they feel that the formulation wasn't disclosed in this particular article.**

Q. **And when you say the formulation --**

A. **I mean all the other ingredients. You have the drug, you have water. What else is in this product, if you will.**

Q. **So let's take it from the perspective of one of ordinary skill in the art.**

What's the first thing your average formulator would do after seeing this article if they wanted to make their own aqueous-based nasal spray for TAA?

A. **I would go, or a person would go to the Physician's Desk Reference, and look up aqueous suspensions of glucocorticosteroid drugs and see if there were any. And obviously we know there was Beconase and there was Vancenase.**

So I would go there. And from looking up into this reference, I could see at least a qualitative list of the ingredients in such a product.

Q. **So if you, just to make sure I understand, if you look up Beconase in the PDR in the prior art, you will get -- what's a qualitative list of the ingredients? What does that mean?**

A. **I am going to see the drug Beconase. I am going to see its dose. And I am going to see a list of the other ingredients. They don't have to put in the quantity. In**

other words, the percentage amount. Sometimes you will get one or two with the percentage in there. But they don't have to put that.

They do have to put the ingredients, though.

Q. From your review of Aventis's development documents, how did they, themselves, create the formulation for Nasacort AQ?

A. Amazingly enough, there is a memo that says that's exactly what they did. They looked at the Beconase formulation.

Q. Why don't we take a look at Defendant's Exhibit 37. Let's make sure we know what we are looking at here at the top. Can you explain that, Doctor?

A. Yes. This is another internal memo, the date was May 17, 1991. And it was written by Drs. Alcorn and Kim. And Kim is the inventor on the patent. And the subject was Nasacort AQ.

Q. Is Dr. Kim the only inventor listed on the patent?

A. Yes.

Q. Does this memo indicate how Dr. Kim developed the ingredient list for Nasacort AQ?

A. I think it does.

Q. Why don't we take a look. As a starting point, you see the second paragraph, all the way down to the ingredient list there?

A. **So basically you can see that the memo says that as a starting point the qualitative formulation for Beconase AQ was used.**

Q. **How would one -- this goes back to the Physician's Desk Reference?**

A. **Yes.**

Q. **Is there -- that's good.**

What else does it show?

A. **Well, what they did is they prepared several different formulations. They weren't sure, as I said, how much of the suspending agent, for example, was there. What the specific quantitative amounts were. So they prepared several different formulations of different weights.**

Q. **So in terms of just the list of ingredients, how closely did Nasacort AQ end up matching Beconase?**

A. **Essentially the same list of are ingredients.**

Q. **Why don't we take a look at Defendant's Exhibit 32. This is something we used in opening.**

You are familiar with this list?

A. **Yes.**

Q. **Explain -- we will get to the details and the ingredients in a second. But explain in general what we are looking at here?**

A. **You can see, we start on the left with essentially the example, which is Nasacort AQ out of the patent. Then we**

have the Beconase AQ, the Vancenase AQ, and the flow Nasacort. So we have three prior art products, and the example from the patent.

Q. Is the ingredient list for these products available in the prior art PDR?

A. Yes, it is.

Q. What is the first line -- I am sorry, the first row underneath the titles?

A. The first row lists or shows the specific drugs. They are all glucocorticosteroids.

Q. The fact that they are all glucocorticosteroids, is that something that has significance to your average pharmaceutical formulator?

A. Well, it tells -- the formulator knows what the physical and chemical properties are from that. Formulators would also know that they behaved similarly, because they are from the same class of drugs. And from looking at the other ingredients, especially the three prior art products, the formulator would know that a successful product has been developed with the glucocorticosteroid and these other ingredients.

He is sitting there saying, boy, I have a high probability of being pretty successful with this.

Q. Now, I want to talk about in a little bit the mixture of MCC and CMC. But just real briefly, what function does

that have in the formulation?
A. It's the suspending agent.
Q. Now, we will move down. benzalkonium chloride?
A. Yes.
Q. What is benzalkonium chloride?
A. That is a preservative. Basically, these are multiple-use sprays. In other words, the patient would get them, I have forgotten how many doses. But they are multiple use. The preservative is in there to essentially kill any microbes that the patient may introduce into the product.
Q. As we go down we see a different -- DETA refers to phenyl ethyl alcohol in the second-to-last row?
A. Yes.
Q. Let's start with phenyl ethyl alcohol. Can you tell me what that is and what it does?
A. That is also another preservative. It is very common when formulating to add a couple of preservative, just to, if you will, enhance your prospects of making sure you kill the microbes.
Q. The combination of benzalkonium chloride and phenyl ethyl alcohol, is that an unusual combination?
A. No, it's a very well-known combination.
Q. So Aventis switched out phenyl ethyl alcohol for EDTA. What is the function of EDTA in the formulation for Nasacort

AQ?

A. **Its major function is also as an additional preservative.**

Q. **Any of different of phenyl ethyl alcohol?**

A. **No. They both work as a preservative.**

Q. **Now, was Aventis the first company to discover that EDTA and benzalkonium chloride could act together as a preservative system?**

A. **No, not at all.**

Q. **Why do you say that? How do you know they are not the first?**

A. **If you would look in the handbook of Pharmaceutical Excipients, every formulator -- there are so many excipients, there is a handbook that lists all the excipients and all of their properties, if you will.**

If you were to look in that handbook, under benzalkonium chloride or phenyl ethyl alcohol you will see that they are used in that way.

Q. **Let's take a look at Defendant's Exhibit 44. And just to put at date on the handbook here?**

A. **This is the 1994 edition.**

Q. **Do you have one of these in your office?**

A. **Yes, I do.**

Q. **Does your average, ordinarily skilled pharmaceutical formulator have one of these available to them?**

A. **Absolutely. There is so many excipients that you can't memorize them all. So you just keep this neat little book to look things up.**

Q. **How long have you had one in your office?**

A. **Years.**

Q. **So now why don't we take a look at the entry for benzalkonium chloride. It is Page 4 in this exhibit. We don't have the whole book in evidence here. Can you pull back so we can see what the ingredient is.**

A. **This is what you would see as the listing for benzalkonium chloride, if you looked it up in that handbook.**

Q. **So this is the preservative in the, one of the preservatives in the prior art products?**

A. **Correct.**

Q. **Does it tell you anything about whether you can combine that preservative with phenyl ethyl alcohol and/or EDTA?**

A. **Yes, it does.**

Q. **Why don't we take a look at the right-hand side.**

A. **So you can see from the highlighted area that you can combine disodium EDTA turbinate, which is EDTA, with benzyl alcohol, or phenyl ethanol or phenyl propanol, to serve as preservatives with the benzalkonium chloride against pseud monastery genosa.**

Q. **Let's break it down just a little bit. I don't see**

phenyl ethyl alcohol listed here as something that can be used in combination with benzalkonium chloride?

A. **I went over it too fast.**

What you say here is, phenyl ethyl in all is phenyl ethyl alcohol, so you have all of these synonyms, it depends on who is writing it what is being called.

Q. **That's the same thing?**

A. **Yes.**

Q. **Literally one line away, the disodium EDTA?**

A. **That is EDTA, yes.**

Q. **I think you did say that?**

A. **Yes.**

Q. **What happens if the pharmaceutical formulator looks up EDTA in the handbook, will that tell them anything about whether it can be combined with benzalkonium chloride?**

A. **Definitely.**

Q. **Why don't we do that. Defendant's Exhibit 44. What is this?**

A. **This is edetic acid, which is the acid form of EDTA, sodium edetate, what we called it before, which is the salt form. The difference is, sodium is a salt, so it's soluble.**

Q. **This is Page 11 for the record.**

Why don't we take a look at the area and typical properties that we decided to highlight here. What is this telling us?

A. **You can see here it says, however, when used with other antimicrobial preservatives, edetate acid or EDTA demonstrates a marked synergistic effect. As you go down it says the edec acids or the edetates are therefore frequently used in combination with such preservatives as benzalkonium chloride.**

Q. **That is the first on the list there?**

A. **Exactly. There is a number of others that you could also see that it is used with.**

Q. **There is reference there of a synergistic effect between EDTA and benzalkonium chloride. Can you tell us what that means, a synergistic effect?**

A. **Yes. That means you are getting a more marked preservative activity than you would expect if you added the two items together. So you get better activity than you would expect.**

Q. **Now, in your review of Aventis's documents, is there anything that talks about whether Aventis itself relied on this synergistic effect disclosed in the handbook?**

A. **Yes. They have a memorandum that basically describes that.**

Q. **Why don't we take a look at Defendant's Exhibit 34?**

A. **Excuse me. It wasn't a memo. It was part of the development report.**

So basically, what the development report is,

the FDA requires that you provide them with information on how you developed your product, what your rationale is, why you put certain things in, why you had certain concentrations. And you put it together in a development report. So they know you understand your product.

Q. Okay. Is there a particular page here, 16, that talks about the issue I had raised?

A. Correct.

Q. Here we go. So what is this showing us?

A. So this is the paragraph where they're talking about their preservatives, so they mention the benzalkonium chloride and the edetate sodium, and then they talked about what we said where you need multiple dosing products requires protection from microbial contamination and growth and they add they used the benzalkonium chloride, which is a GRAS excipient and it's effective, does not have any odor and then they use the EDTA because it had been shown to have a synergistic effect.

Q. What does a GRAS excipient mean?

A. GRAS means it's kind of a designation meaning generally regarded as safe. In other words, the FDA knows it's okay. And if you are going to use any ingredients, usually I try to use GRAS excipients because you know you won't have to argue with the FDA about.

Q. Okay. Well, maybe Aventis was the first company to

use this combination of benzalkonium chloride and EDTA in a nasal product.

A. No, not at all.

Q. How do you know that?

A. Because we looked in the PDR and basically there are a number of products with the combination of benzalkonium chloride and EDTA.

MR. HURST: And we prepared a demonstrative exhibit is to help us with this. Can we pull up No. 30?

BY MR. HURST:

Q. So what are we looking at here?

A. You can see here there are eight products. And these eight products have the combination of EDTA with benzalkonium chloride. We looked in the PDR, as I said, and found these products.

Q. And what kinds of product are these? Are they nasal products?

A. Yes, they're nasal products.

Q. Nasal products. Okay. You understand Aventis's argument with respect to these products, that these are solutions and the claimed invention is a suspension? You understand that?

A. Yes, we discussed that some.

Q. Okay. Here is my question for you. First, it's probably not necessary but, very quickly, what is the

difference between a suspension and a solution?
A. In a suspension, the drug is not completely soluble to give the dose that is necessary to be therapeutic so you have essentially to get the whole dose in. You have to suspend some of the drug as powder. So you have dissolved the dose drug as much it can dissolve and then you have the drug suspended. The rest of the dose is suspended.
Q. All right.
A. Contrast it to a solution where it's all dissolved. All the drug is solubilized.
THE COURT: I expect that is the last time he is going to ask that. We'll see.
MR. HURST: I'm sorry, Your Honor. I rethought that as soon as I asked it.
BY MR. HURST:
Q. Now, does it make any difference with respect to the usefulness of EDTA and benzalkonium chloride that these nasal products or are solutions and the claimed nasal spray is a suspension? Does it make any difference?
A. No, the designation of the dosage form as a suspension or a solution refers to the drug. The EDTA and benzalkonium chloride are soluble in the water. That is essentially the vehicle. And for them to work, they have to be dissolved in that water. Whether it's dissolved in the water that ultimately is a surfactant or dissolved in water that is a

solution, it doesn't matter. They work.

Q. **You have heard discussion about or at least the suggestion that choosing EDTA was nevertheless an invention because it doesn't have a scent. I want to ask you a few questions about that. Was it known in the prior art that EDTA had no scent?**

A. **Yes.**

Q. **How was it known?**

A. **I think you could look at the Handbook For Excipients. I think it's defined in there.**

MR. HURST: So why don't we pull that back up, Defendant's Exhibit 44, Page 12.

BY MR. HURST:

Q. **So just for the record, this is the Handbook of Pharmaceutical Excipients?**

A. **Yes. This is the same page that we saw the title page before.**

Q. **And?**

A. **This is the EDTA, disodium edetate. And with reference, it describes the appearance as being an odorless white crystalline powder.**

Q. **How about you, yourself, as a person working in this field? When were you aware that EDTA didn't have a detectable scent before Aventis started its work in 1991 or 1992?**

MR. RICH: Your Honor, this is beyond the scope of the expert report, the scented or scentless nature of EDTA.

MR. HURST: I believe that is in the expert report. Yes.

I apologize. I hadn't prepared for this because I thought it was in there for sure.

(Pause.)

MR. HURST: Paragraphs 86 through 89 all talk about the odorless requirement.

MR. RICH: Your Honor, they talk about whether phenylethyl alcohol in a product is odorless. They don't talk about EDTA in any way in terms of odor.

MR. HURST: That's the --

MR. RICH: And if I could -- well --

THE COURT: Do you want to talk about it?

MR. HURST: Yes.

(The following took place at sidebar.)

THE COURT: Let me ask a question. Aren't we talking about equivalent agents?

MR. RICH: No, Your Honor, we're not. And that is something we are going to establish.

THE COURT: You say that, but he says they are. He is the expert.

MR. RICH: Well, Your Honor, I took his

deposition. I think we'll hear him say on cross-examination that the primary use of EDTA is as a chelating agent, not as a preservative. In fact, this is incorporated into this product as a chelating agent. Furthermore, this is a product in which EDTA that was never used, to his knowledge, in a nasal suspension. And we do submit that that is an important issue.

THE COURT: It sounds like you can do a good job of cross-examining the doctor.

MR. RICH: Thank you, Your Honor.

THE COURT: Overruled.

(End of sidebar conference.)

BY MR. HURST:

Q. Did you, yourself know that EDTA was odorless before Aventis came along in 1991 and 1992 with its Nasacort AQ?

A. Yes, I did. I used it a number of times.

Q. All right.

A. And mostly in injectable type preparations.

Q. EDTA also has a second function in the formulation. Is that true, doctor?

A. That's true, yes.

Q. What else does it do?

A. EDTA really works by being a chelating agent. And what that means is if there are any stray ions left over, it scoffs them up, it takes them out of play. And by doing

that, it has the ability to stop oxidation reaction. So it enhances the stability of, say, a drug that degrades by oxidation.

THE COURT: Just dissolving into the air, or what is oxidation?

THE WITNESS: No. Oxidation means simply if there are oxygen molecules in the formulation, in other words, there would be water, oxygen, the drug could oxidize and degrade. You know, the drug would break down and would lose its concentration.

THE COURT: Okay.

THE WITNESS: So it just stops this happening.

BY MR. HURST:

Q. Well, was it known in the prior art that EDTA could act both as a preservative and as an antioxidant?

A. Yes. As a matter of fact, it was probably used more as an antioxidant than as a preservative.

Q. Is that disclosed anywhere in any common reference books?

A. Again, in the handbook, yes.

MR. HURST: Why don't we take a look at that. Defendant's Exhibit 44, Page 11.

BY MR. HURST:

Q. This is the entry for EDTA?

A. Correct.

MR. HURST: All right. Why don't we take a look at the column under technology, second paragraph. If you highlight, let's say, the first six lines or so, so we can read it.

BY MR. HURST:

Q. **What does this tell you, Dr. Needham?**

A. **Well, basically what I just explained. And that is the fact that it is often used as an antioxidant because it sequesters trace amounts of metal ions that will catalyze autoxidation reactions.**

Q. **Okay. So let's return to the scent issue again. And particularly I want to ask you about phenylethyl alcohol. Phenylethyl alcohol, you understand it has a scent?**

A. **Yes.**

Q. **What is that?**

A. **It's a rose scent.**

Q. **And was is your understanding about whether phenylethyl alcohol is an ingredient that qualifies as an odorless ingredient under the Court's claim construction? Actually, it's the parties-agreed-to claim construction.**

A. **Well, I think as I said, or as you just said, it's the agreed-to claim construction says that it would be acceptable if it didn't cause discomfort to the patient.**

MR. HURST: Let's take a look at Defendant's Demonstrative Exhibit 68. I hope I have the right number.

Demonstrative exhibit. There we go.

BY MR. HURST:

Q. **All right. So you don't have to memorize it. We have the agreed claim construction up there.**

A. **Correct.**

Q. **Now, what is your understanding under that claim construction as you understand these ingredients as a person who has been in this industry for awhile? Are EDTA and phenylethyl alcohol odorless?**

A. **By the criteria of the agreed claim construction, definitely.**

Q. **How do you know phenylethyl alcohol is odorless? It has a rose scent. Isn't it possible that causes users discomfort?**

A. **Well, if you look at the patent, the patent basically says that the construction or the composition will have to be something that would not cause discomfort to the patient. So I think if you bring --**

MR. HURST: Why don't we do that? Why don't we pull the patent up. It's Defendant's Exhibit 7. And we'll take a look. You have already done it.

THE WITNESS: There you go.

BY MR. HURST:

Q. **So this is what you are referring to?**

A. **Yes.**

Q. **Why don't you explain to Judge Sleet, this is Column 1 from Defendant's Exhibit 7. Right?**

A. **Yes. So this is from the '573 patent and it says, other desired characteristics of the pharmaceutical composition are that it not contain ingredients which cause the user discomfort.**

Q. **And does the patent anywhere else, given this statement, indicate whether phenylethyl alcohol is an acceptable ingredient?**

A. **Yes. Later in the specification, it defines or it lists some acceptable ingredients of which phenylethyl alcohol has to be an acceptable ingredient.**

MR. HURST: Let's take a look at Column 6.

A. **So, here, you can see that examples of pharmaceutically acceptable antimicrobial agents that can be used in a composition include, benzalkonium chloride, a whole series of others, and then we finally get down to, chlorobutanol and phenylethyl alcohol.**

Q. **So just in summary, as a person of ordinary skill in the art -- and obviously you are above one of ordinary skill in the art but I want to ask you to take the perspective of one of ordinary skill in the art. Is it inventive in the context of these nasal sprays to use a benzalkonium chloride EDTA combination rather than a benzalkonium chloride/phenylethyl alcohol combination?**

A. **Not at all.**
Q. **And just briefly, what is your reaction to the suggestion that it is inventive?**
A. **I don't think it is inventive at all. We've seen the evidence that was known and easily attainable knowledge to somebody of ordinary skill in the art. All they had to do was look in the handbook.**
MR. HURST: Okay. Let's take a look back at Defendant's Demonstrative Exhibit 32.
BY MR. HURST:
Q. **We looked at this before. And now I want to turn to, in particular, the mixture of MCC and CMC. We've heard discussion in the proceedings about these two ingredients. Correct?**
A. **Correct.**
Q. **And all the prior art formulations have it?**
A. **Yes.**
Q. **Now, here is my question. What is the function of these ingredients in the context of these thixotropic nasal sprays?**
A. **Okay. What you want in this type of nasal spray is something that is going to be thick enough to hold the suspension suspended and homogenously suspended so, you know, within a unit volume of liquid, you have to the same dose every time. Okay?**

The other piece of the equation, if you will, or requirement is you want it to be able to be sprayed out of the spray pump into distinct droplets. So that is really what you want from your suspending agent.

Q. **So it is thick enough to suspend --**

A. **Thin enough to spread.**

Q. **Was this known in the prior art, that MCC and CMC could provide nasal sprays with this quality, being thick enough to spread and thin enough to spray?**

A. **Definitely, because it's used in Beconase, it's used in Vancenase and it's used in Flonase. Those are successful nasal suspensions.**

Q. **Now, without going through the time of pulling out the claims, you understand this patent, however, has a particular ratio, with a ratio of MCC 85-to-95 percent of the mix of the two; right?**

A. **Correct.**

Q. **Here is my question for you. Is there anything unique or novel about having a mixture of MCC and CMC where MCC is 85-to-95 percent of that mixture?**

A. **No. As a matter of fact, you can go to FMC. If you combine the two products, it's called Avicel, as you have heard. You go to FMC and they sell the Avicel within those concentration ranges defined in the patent.**

Q. **What is FMC?**

A. **It's a company that is one of the major suppliers of excipients to the pharmaceutical industry.**

MR. HURST: All right. So let's take a look at a FMC brochure. Defendant's Exhibit 42.

BY MR. HURST:

Q. **What are we looking at?**

A. **This is one of their advertising pieces, if you will. All of the excipients manufacturers provide these to help the formulator; and it defines for the formulator the characteristics of what they're trying to sell.**

Q. **What is the date of this product brochure?**

A. **I believe it's 1993.**

Q. **And that's on Page 11?**

A. **Yes.**

MR. HURST: Let's take a look at the chart on Page 3. Just so we can see it, can you blow up two Avicels 591 and 611 on that top chart?

BY MR. HURST:

Q. **Can you explain what this product brochure is telling folks about Avicel?**

A. **Yes. You can see Avicel 591F and CL-611 and the percent MCC is 88 in the 591 and 85 in the 611. So it fits within the defined range.**

Q. **Was Aventis the first to actually buy this commercial product, Avicel and put it into a nasal spray?**

A. **No. As a matter of fact, if you go to the Flonase list of ingredients, it shows that they're using the 591.**

MR. HURST: Why don't we go do Defendant's Exhibit 18, Page 2.

A. **So you can see here, they talk about the microcrystalline cellulose and the carboxymethylcellulose, and underneath they call it Avicel 591. It's the product we just talked about.**

Q. **And does that active ingredient help you identify what product we're talking about?**

A. **Yes, the fluticasone which is the Flonase.**

Q. **Now, it looks like obviously Flonase uses 591 but Aventis uses a different off-the-shelf product, 611; right?**

A. **Correct.**

Q. **Is that significant to one of ordinary skill in the art?**

A. **No.**

Q. **Why not?**

A. **Basically what the person is going to do is given the requirements that I have described before, you know, the thick enough to suspend and thin enough to spray, they're going to try different combinations to see how they're going to mix them, what percentages, if you will, of the microcrystalline cellulose and the carboxymethylcellulose will give them the best to fit those characteristics.**

Q. **And do you happen to know what Beconase and Vancenase uses? Do they use the commercial off-the-shelf products or do they actually use their own CMC and MCC?**

A. **I don't know. I've never been able to discover, if you will, which they use but given the difficulty of mixing the two and getting them to be a reproducible product, I'm sure they just buy it. That way, they can just buy it and put it into the mix when they're making it in the factory. So it's too much in a pain in the neck to get them right.**

Q. **So how about Aventis, do you know what they did? Did they mix it themselves or did they buy it off of the shelf?**

A. **There is a memo that describes it but basically they started mixing it themselves.**

MR. HURST: Let's take a look at Defense Exhibit 34.

BY MR. HURST:

Q. **Okay. We're looking at the --**

A. **Yes, we're back to the development report, essentially.**

MR. HURST: Why don't we take a look at Page 15 of the development report. Can we highlight the third? You got it. That is what we need.

BY MR. HURST:

Q. **Can you explain what we're looking at here, Dr. Needham?**

A. **This is the paragraph that basically talk about the they did with the microcrystalline cellulose and the carboxymethylcellulose. The highlighted portion basically says that they found that certain combinations of the microcrystalline cellulose and the carboxymethylcellulose were acceptable but they stopped or abandoned making those combinations because they had, it took too long to make a consistent suspension. When you make these pharmaceutical products, you are always on a time constraint and so, you know, time is money. You got to get it done and you can't have any variability. So you just buy Avicel.**

THE COURT: So like ANDA litigation.

THE WITNESS: Pardon?

THE COURT: Sort of like ANDA litigation.

THE WITNESS: Yes.

BY MR. HURST:

Q. **So what do they do then?**

A. **So basically they got themselves some Avicel 591 and some Avicel 611 and said, okay, now we're going to make some of these and see what we can do to find something that fits our criteria.**

Q. **And so when they examined those two different products that they bought from FMC, what did they determine about whether or not that would produce acceptable nasal sprays?**

A. **They found that both of them worked.**

Q. **And where do we see that?**

MR. HURST: If we take a look at -- there we go. Bottom of the Page 15, top of Page 16.

BY MR. HURST:

Q. **What are we looking at here?**

A. **So again they're just describing essentially what they found out when they tried different concentrations of the 591 and the 611 and they finally settled on a concentration of each. And it said basically that the setting viscosity was high enough to hold the particles suspended in the bottle. And later, they said the shaken viscosity was low enough to deliver the target amount out of the pump as a fine mist, which is essentially what they're objective was, if you will, that we described earlier.**

MR. HURST: Why don't we highlight on Page 16. Can we go to Page 16?

BY MR. HURST:

Q. **Did they make a determination, Dr. Needham, about whether or not both of those Avicel product would produce a nasal spray that fit the viscosity claims in the patents at issue?**

A. **I believe they did, yes.**

MR. HURST: Okay. Why don't we take a look at, why don't we highlight the top paragraph and see if it's good enough, if it's big enough to read.

BY MR. HURST:

Q. **Is there something in this paragraph that shows that they determined that both Avicel 591 and 611 met the viscosity requirements?**

A. **Yes. Let's see. We talked about the 591 ranging from one to 1.3 percent. And then the Avicel about 2.3 percent. And that gave --**

Q. **Next sentence.**

A. **It was determined that the viscosity of these suspensions was 100 to 200 centipoises after the suspension and 500 to 1,000 centipoises when the suspension was not shaken. So that is essentially the range that we have in the patent.**

MR. HURST: So why don't we take a look now at -- and why don't we take a look at Claim 5 of the patent, of the '573 patent. DX-7. Got it?

BY MR. HURST:

Q. **Now, I'm going to focus on the unsheared and sheared viscosity measurements here. Is there any magic to these numbers to one of ordinary skill in the art with the ability to make up a nasal spray?**

A. **No. As a matter of fact, if you look at what actually happened with the formulator, they did, in the last paragraph, determine those concentrations. They determined that it worked. In other words, it suspended properly,**

sprayed properly. And what it actually says in all that verbiage, then we determine what the viscosity was. So they kind of worked backwards.

Q. **Did you see anything in the development report that you read or in any of the other Aventis documents that you read that they were attempting to pick viscosity profiles that would enable a nasal spray to reach the frontal sinus?**

A. **No.**

Q. **Did you see any reference in the development documents to the nasal spray reaching the frontal sinus?**

A. **No.**

Q. **Now, on this third point here, it talks about the viscosity of the nasal spray in the deposited form; right?**

A. **Yes.**

Q. **And we had Dr. Donovan talk about that and I'm not going to repeat that. I just have one question for you. Given your knowledge of the Beconase formulation, the Flonase formulation, the Vancenase formulation, and the Nasacort formulation, would you expect them to behave any differently in the nose?**

A. **No. Essentially, they have the same type of drug. They have the type ingredients in the same pretty much composition. They are sprayed out of a spray pump that is very similar. I would expect them to all behave just about exactly the same.**

Q. **All right. So now, just to sum up, Dr. Needham. With respect to Claim 6 of the '573 patent, and Claim 26 of the '329 patent, what is your opinion with respect to whether or not those claims are obvious over the available prior art?**

A. **They would be obvious, I think, to someone skilled in the art. I think basically as I said, you have the similar type drugs. You have the ingredients. You have the same spray pump. You see products that have been converted from aerosol to aqueous suspensions. And you have seen that they're successful from a clinical or therapeutic point of view. So as you are sitting there, if you were me at that point in time, you would know that you could do this.**

MR. HURST: Thank you, Dr. Needham.

THE COURT: Thank you. You may cross-examine, counsel.

MR. RICH: Thank you, Your Honor.

CROSS-EXAMINATION

BY MR. RICH:

Q. **Hello again, Dr. Needham.**

A. **Hello.**

Q. **How are you?**

A. **I'm doing fine. I'll let you know in a little while.**

Q. **Well, hopefully you can let me know right up front.**

MR. RICH: If I could approach, Your Honor?

THE COURT: You may approach.

THE WITNESS: I'm certainly not rushing to make a plane this time. We had that issue in my deposition, Your Honor.

(Documents passed forward.)

BY MR. RICH:

Q. **I've just handed you an article entitled In Vivo Evaluation of Sprayed Formulations of Human Insulin For Nasal Delivery. Correct?**

A. **Correct.**

Q. **And you are one of the named authors.**

MR. RICH: If we could bring it up on the screen, please.

A. **That is true.**

Q. **And this was, this article was received, was written as of November 30th, 1994; right?**

A. **Correct.**

Q. **And then it was published in 1995?**

A. **Yes. Some time after the 1st of February.**

Q. **Some time after the 1st of February. And if you could turn to page 92 of that article for me. And look in the right-hand column, there is a paragraph there in the middle of the page, that says:**

It was reported earlier that by increasing the viscosity of nasal formulation, one can significantly increase the residence time of drug at the site of

deposition.

Do you see that?

A. **Yes.**

Q. **And you cite seven different articles for that point. Right?**

A. **Several, yes.**

Q. **Seven?**

A. **Several? Are there seven?**

Q. **Two Morimoto, a Pennington?**

A. **I see four.**

Q. **Two Morimoto, Pennington, Harris three times and Lin?**

A. **Okay. Six of one-half dozen of the other.**

Q. **Well, seven of one in this case?**

A. **Sorry about that.**

Q. **Then you say visco-bioadhesive formations having suitable requirements can be formulated but such systems would not be easily administered to the nasal cavity with the existing drug delivery devices. Right?**

A. **That's true.**

Q. **And those two sentences reflect your then current thinking as of the publication of this article in 1995?**

A. **Yes.**

Q. **And supported by the seven articles you cite. Right?**

A. **Well, no. I think the seven articles talk about the deposition.**

Q. **Fair enough. Not the second point. It's the first point?**

A. **Correct. I am glad to see you have been reading all of my publications.**

Q. **I am a big fan.**

This is an article entitled Bioadhesive and Formation Parameters Affecting Nasal Absorption. Correct?

A. **Yes.**

Q. **This is a review article. And you are one of the authors on this review article?**

A. **Correct.**

Q. **Now, as a review article, you were attempting to set forth with the greatest accuracy what was known in the art at the time it was written. Right?**

A. **Yes.**

Q. **And this article was revised and accepted in May 1995?**

A. **Yes.**

Q. **So it's pretty closely an approximation of what was thought by formulators as of the critical date of July 1995. Right?**

A. **Correct.**

Q. **Now, if you turn to Page 118, one of the formulation parameters you discuss on the section bridging 118 to 119 is viscosity. Correct?**

A. **Yes.**

Q. **And after reviewing several articles, you reached the ultimate conclusion on Page 119, it says, Thus, increased viscosity prolongs the retention time of drug in the nasal cavity, but whether this will result in improved absorption of drugs or not remains unclear.**

Right?

A. **Yes.**

Q. **So in general, a person of ordinary skill in the art in 1995 might have thought that increased viscosity would prolong retention time of drugs in the nasal cavity but would have understood that you cannot predict the bioavailability of a drug based on the viscosity of a formulation that uses methylcellulose as the viscosity enhancing agent. Right?**

A. **I don't see -- well, a number of -- we talked about a number of different excipients that enhance viscosity, sure.**

Q. **My question is whether, in general, a person of ordinary skill in the art in 1995 might have thought that increased viscosity would prolong retention time of drugs in the nasal cavity but would have understood that you cannot predict the bioavailability of a drug based on the viscosity of a formulation that uses methylcellulose as the viscosity enhancing agent?**

THE COURT: I think, counsel, you could break that down. That's more than one question. There is more

than one question in there, at least as I hear it. I think the questions are appropriate. I would suggest you reformulate your question.

MR. RICH: We would contest that reformulation is really important in this case.

(Laughter.)

BY MR. RICH:

Q. A person of ordinary skill in the art in 1995, that is the shoes you are in, they might have thought that increased viscosity would prolong retention time. But they would have understood that that is not predictable. Right?

A. That's true.

Q. And you have been here in the courtroom listening to some of the testimony. Correct?

A. Yes.

Q. And you have heard about the viscosities of Nasacort AQ and Barr's ANDA product and Flonase. Right?

A. Yes.

Q. And Flonase is higher than Nasacort AQ or Barr's ANDA product?

A. I have seen some numbers, yes.

Q. You know, I would like to talk for just a little bit about the approach you took --

THE COURT: I didn't mean to throw you off the MCCs.

MR. RICH: I will go back to the MCCs. Thank you very much, Your Honor.

THE WITNESS: Appreciate that, Your Honor.

BY MR. RICH:

Q. **We are talking about a methylcellulose-based system here with Nasacort AQ. Right?**

A. **It's a combination system. Methylcellulose and carboxy methylcellulose.**

Q. **And in that sort of system, the person of ordinary skill in the art in 1995 would have thought this increased viscosity might prolong retention time, but would understand that you can't predict it?**

A. **That's true.**

MR. RICH: Thank you, Your Honor.

BY MR. RICH:

Q. **Now turning to the approach that you took in the obviousness analysis. The definition of thixotropic, the claim element thixotropic that you used in forming your obviousness opinion, that's what I want to focus on. Now, that definition of thixotropic that you used in the obviousness analysis was a liquid or a liquid system that has a high viscosity at rest, when shear is applied to it, it has a decrease in viscosity, and then, as a function of time, it returns to the original high viscosity. That's correct. Right?**

A. **Correct.**
Q. **And in your definition that you used in your obviousness determination, your definition of thixotropic, there is definitely not immediate recovery. Right?**
A. **That's true.**
Q. **But the lawyers, Barr's lawyers in this case, provided you an appendix of claim terms. Right?**
A. **Yes.**
Q. **For use in this case. And they represented to you that these were the Judge's construction of claim terms. Right?**
A. **Correct.**
Q. **And that was appended to your report as Appendix A.**
Could I get a verbal answer?
A. **I said yes. I thought I did. Okay.**
Q. **I apologize if you said yes and I missed it.**
Now, there were details in the definition that was in Appendix A. What the lawyers told you was the Court's definition that was not in the definition that you applied in determination obviousness. Is that correct?
A. **I don't believe so. But we could look at it.**
Q. **Well, let's first look at it. I believe it's on the second page. This is the definition you were provided by counsel. Right? On the second page?**
A. **Correct.**

Q. **And there were details in this definition, what the lawyers told you was the Court's definition of thixotropic that were not in the definition that you applied in determining obviousness. Is that correct?**

A. **Let me look at this, please?**

Q. **Sure.**

(Pause.)

A. **I don't know if I agree with you there.**

Q. **Okay. Well, let me show you, as soon as I can make another round trip with my workout for the day, let me have you turn to Page 176 of this transcript. And you were asked, maybe you can even try to play it. We paid all this money. We might as well see if it works.**

"Question: And there are things in the definition that you applied in terms of thixotropic that were not in that general definition. Is that fair to say?

"Answer: No. I guess I probably misspoke before. I think I would have gone with the more simple definition of thixotropic, the second one I just gave you, where it's thick at resting. When you add shear, it decreases. And then, when you let it rest, it goes back to being the same viscosity as a function of time.

"Question: I think I understand that you're saying that a previous answer may have been unclear, so I'm -- I'm, you know --

"Answer: Okay.

"Question: -- unclear in understanding. So if you could tell me in your obviousness analysis what the definition of thixotropic you used was?

"Answer: Okay. The short form of what I think has been used as thixotropic was a liquid or a liquid system that has a high viscosity at rest. When shear is applied to it, it has a decrease in viscosity. And then, as a function of time, it returns to the original high viscosity.

"Question: And you said that was the short form of what you used. Were there any other details?

"Answer: No.

"Question: And there are details in the definition of Appendix A that weren't in the definition that you applied in determining obviousness?

"Answer: That's right.

"Question: Dr. Needham, before the break, we were talking about thixotropic" --

MR. RICH: That's enough.

BY MR. RICH:

Q. **If you could just look, I think we confirmed again, if you turn to Page 177 -- I am sorry, turn to Page 176, your answer continued, "I used a general, what I call a general definition of thixotropic as opposed -- this is a -- the definition as my understanding, it's the definition approved**

by the Court that's specific to the factors and parameters and issues involved in this patent suit.

"Question: But you didn't use that in the obviousness analysis.

"Answer: That's correct."

So your testimony was that you did not use the Court's definition of thixotropic in your obviousness analysis. Is that a correct summary of your testimony?

A. I think the --

Q. Was that your testimony?

A. That was my testimony.

Q. Okay. The asserted claims, the two asserted claims --

THE COURT: Did you want to explain that?

THE WITNESS: I would like to. But I didn't know that I could.

THE COURT: I would like you to as well, yes.

THE WITNESS: Okay.

Basically, my testimony, as I understood it when I was giving it, was the fact that I was looking at the requirements using the definition of thixotropic as the requirements that a formulator would use, a person of skill in the art would use, when they were formulating that product. In other words, the thick viscosity, being sheared to be thin enough to spray, and then returning in vitro back.

Now, I wasn't focusing on it having the exact numbers that are provided in there. Actually, you know, the 400 to a thousand when it's at rest, and then the 50 to 200 when it was sheared. I think, as we saw from the development report, neither did the formulator for Aventis. After the fact they determined what those viscosities were.

THE COURT: Go ahead.

BY MR. RICH:

Q. **I heard you just tell His Honor this. But you did not in your obviousness analysis pay attention to the exact viscosity numbers required by the claims. Correct?**

A. **That is correct.**

Q. **So you didn't look to see whether the unsheared viscosity was between 400 and 800 centipoise. Right?**

A. **Unsheared viscosity where?**

Q. **I am sorry. You did not look to see whether prior art references had unsheared viscosities between 400 and 800 centipoise in your obviousness analysis. Right?**

A. **Well, I certainly reviewed the prior art references and didn't see any reference to unsheared viscosity or sheared viscosity. It just wasn't presented in that way.**

Q. **You just didn't pay attention to what the specific numbers associated with any viscosities were?**

A. **I think I read the references. If I had seen that they had provided specific numbers, I would have paid**

attention, if you will. I would have noted that. It was never presented in that way. It's just not a way that a pharmaceutical formulator considers or presents it. You are developing a product that has to have certain outcomes to become an acceptable product to the FDA, and for therapy. The numbers are incidental, if you will.

I realize we have made a big deal of them in this case. But they are not -- you know, they sort of are related to the fact that the product must behave in a certain plan. But they are not the primary thing that's in the mind of a formulator when they are making this product or formulating this product.

Q. And you saw no testing results that you used in the obviousness analysis to say, this has a viscosity of 400 to 800 centipoise in unsheared form. Right?

A. That I used or that I read?

Q. That you used in your obviousness determination.

A. I didn't use any. I read things and analyzed them.

Q. But none of that set forth whether there was a viscosity between 400 and 800 centipoise?

A. No, nowhere was there defined the viscosity in that manner.

Q. Nowhere was there defined the viscosity in the sheared form between about 50 and about 200 centipoise?

A. No. They just talked about it being thick enough to

suspend it and thin enough to shear.

Q. Again, in terms of deposited form on the nasal mucosa, nothing about the prior art products that you read said that they would have a viscosity between about 400 and about 800 centipoises. Right?

A. No.

Q. Now, in your testimony on direct, you relied upon Defendant's Exhibit No. 34, the PPIS statement.

A. Yes.

Q. This isn't a prior art document, is it?

A. No.

Q. And this isn't information that would have been available to a person of ordinary skill in the art, would it?

A. Definitely not.

Q. And when you talked about the experiments that, I believe it was Rhone-Poulenc Rorer at the time, did in relation to after-cell suspensions, that was something that they had kept confidential to your knowledge. Right?

A. What experiments?

Q. If we can turn to Page 16. If you go to the top paragraph before dextrose, you had some testimony about the experimental work that was done at Rhone-Poulenc Rorer with regard to Avicel RC 591 and Avicel CL 611. Do you remember that testimony from direct?

A. **Yes.**

Q. **But this information was not available to a person of ordinary skill in the art in 1995. Correct?**

A. **That's true. However --**

Q. **Well, I have got limited time.**

A. **Okay.**

Q. **I am sure you will be asked a bunch of questions on a bunch of these.**

One of the other documents that you consulted pretty heavily was Defendant's Exhibit 33. This was a March 1st, 1991 memo?

A. **Yes, the rationale.**

Q. **And this isn't something that a person of ordinary skill in the art would have had. Right?**

A. **No. It was an internal document.**

Q. **And they wouldn't have known what was set forth in this internal document?**

A. **Pardon?**

Q. **They would not have known what was set forth in this internal document. Right?**

A. **No.**

Q. **Another document that you relied upon was Defendant's Exhibit 37. And this is the Nasacort AQ memo from Dr. Alcorn and Dr. Kim. Again, this was an internal RPR document. Right?**

A. **Correct.**
Q. **And people outside of RPR, people of ordinary skill in the art, would not have known about this document. Right?**
A. **Well, this was just shown.**
Q. **Would they have known about this document?**
A. **No.**
Q. **Would they have known what was in this document?**
A. **No.**
Q. **So this information was not available to a person of ordinary skill in the art?**
A. **Well, there is where I disagree. The information about the formulation was available, and this was just given as a backup.**
Q. **The information about what RPR scientists were trying internally, confidentially, was available to a person --**
A. **The qualitative list of ingredients was.**
Q. **The qualitative list of ingredients that those people were using experimentally, your testimony is that was available to a person of ordinary skill in the art?**
A. **Yes, it says, as a starting point the qualitative formulation for Beconase AQ was used. That's in the PDR. That's what they used.**
Q. **I apologize. I wasn't suggesting the qualitative formulation of Beconase AQ. You also testified about a qualitative list of ingredients that was used in early**

development at RPR. Right?
A. Well, I thought they were one and the same.
Q. Well, Beconase AQ didn't use triamcinolone acetonide, did it?
A. Well, that's true.
Q. To your knowledge, you don't know one way or the other whether it uses Avicel RC, mixture of CMC and MCC. Right?
A. Other than my own experience that tells me it had to.
Q. It had to have been?
A. Yes. It had to have been used. I would think simply because of the same problems that were defined in other issues, and that's the fact that it's such a pain in the neck to mix these two together to get reproducible suspension that, you know, you are going to buy something, that you can do it as a no-brainer.
Q. But they didn't have to do that. Right?
A. No, they didn't have to.
Q. And there is nothing in their product information that says they did that. Right?
A. In whose product information?
Q. In the Beconase AQ product information?
A. No.
Q. You testified earlier about who would be making inventions in this area, whether it would be an individual formulator or a group of people. Right?

A. **Yes.**
Q. **And you said that one person would ultimately be responsible for the formulation. I believe that was your testimony. I was trying to madly scribble it down, so I don't know if I got it correctly. Is that basically the gist of your testimony?**
A. **Yeah, by responsible I meant that there would be one person who would be formulating it.**
Q. **But they would be part of a project team in the formulation process, wouldn't they?**
A. **They would be part of a project team that was used to develop the product.**
Q. **And that project team that was used to develop the product would be making decisions jointly as to whether the product was an appropriate product or not. Right?**
A. **But they wouldn't be telling the formulator --**
Q. **Is that --**
THE COURT: Let him answer the question.
THE WITNESS: They wouldn't be telling the formulator what he was supposed to put into the formulation.
BY MR. RICH:
Q. **Is that your testimony today, that the project team would not direct what the formulation would be?**
A. **Specifically, they would not direct the exact details of the formulation, no.**

Q. **But they might very well impact whether, for example, a solution were developed for a suspension. Right?**

A. **Well, it would be impossible to develop an aqueous solution of this drug.**

Q. **It would be impossible to develop an aqueous solution of this drug?**

A. **Correct.**

Q. **Are you familiar with the drug Nasalide?**

A. **That's not an aqueous. It's a co-solvent.**

Q. **What is the ultimate base, what is the largest recipient in Nasalide?**

THE COURT: I guess my question is, is that relevant, this line of inquiry relevant to my considerations?

MR. RICH: Your Honor, I believe it is.

BY MR. RICH:

Q. **What is the basis --**

A. **Well, there is water in it. I don't know the percentages of all of the co-solvents off the top of my head.**

Q. **And Nasalide was in existence in 1995. Right?**

A. **Certainly.**

Q. **And that's a development route that a formulator could have followed, creating a -- is a co-solvent system a better description?**

A. **Yes. I think the formulator would have known that a co-solvent system, with the solvents necessary to dissolve that drug, would have been irritating and it was generally known in the art that it was irritating to the patients and would have not gone down that road.**

Q. **So a formulator in your mind would not have developed a products, would not have followed down a road towards a drug that causes irritation. Is that your testimony?**

A. **They would try their best not to.**

Q. **If I could get the Beconase package insert. I believe you have the Beconase package insert in your --**

A. **In my book?**

Q. **We have got an NDA excerpt. We don't have the package insert.**

Were you here earlier during Dr. MacKay's testimony?

A. **Yes.**

Q. **And did you hear him testify that according to the package insert the primary side effect of Beconase AQ in 24 percent of patients was nasal irritation?**

A. **I will have to defer to you on that. I wasn't noting that it was 24 or that it was...**

Q. **Here we go. Here is the language in Beconase AQ. So your testimony is that you wouldn't have followed the Nasalide path because of nasal irritation. But it's correct**

that Beconase AQ has a side effect of mild nasopharyngeal irritation, in up to 24 percent of patients treated. Right?

A. I mean, with all due respect, I think, basically, if you look at any of these, there are people in the population who would show irritation.

You know, so, is the 24 percent, it says mild pharyngeal irritation, you know, is that a significant number? I mean, I am not a physician. I am a formulator.

Q. But your testimony was -- and correct me if I am wrong -- that a formulator or a project team would not go down the route of Nasalide because of irritation. Right?

A. That's right. The Nasalide had major irritation issues.

Q. And Beconase has irritation issues as well. Right?

A. Every one of these products have irritation issues.

Q. Well, could we look at the Nasacort AQ package insert.

A. While we are waiting, I can give you a testimonial on Nasacort AQ. My wife is very allergic. When I was discussing the case with her, she mentioned the physician had to take her off Nasacort AQ because she had irritation issues. It's just a little testimonial to fill in the time.

MR. RICH: Your Honor, I would ask that be stricken from the record.

THE COURT: It is stricken.

BY MR. RICH:

Q. **While we are waiting for the Nasacort AQ package insert, your testimony, your opinion, earlier on, that someone would not go down the nasal irritation route of Nasalide, was based on the project team rejecting Nasalide as an option. Right?**

A. **Well, I think the formulator, you know, of ordinary skill in the art, would be aware of the fact that the co-solvent system, Nasalide product, had caused irritation issues.**

Q. **Why don't we focus on your testimony in your deposition then. And turn to Page 127 of your deposition.**

Looking at Page 127, you were asked:

"And in your mind, a person of ordinary skill in the art in 1995 would go so far as to reject the approach of a solution based on irritation or burning demonstrated by Nasalide?"

You said, "I would say the project team would, but it would get rejected."

And the question was, "Well, when you say a project team, I am trying to figure out the obviousness determination that you did. In doing the obviousness determination, did you look from the point of view of an individual or a project team?

"The individual, but I guess I'm caught in my corporate persona because no individual makes a single

decision on that level. They would -- it would be the responsibility of the person of ordinary skill in the art who had responsibility to formulate, to bring to the project team, here's what I found in the literature. And, you know, it's a no-brainer. The marketing guy would sure as heck knock you, if not everybody in the room."

Right?

A. **Yes.**

Q. **And that's the reason that you rejected the pathway of Nasalide.**

The next question was: "And the person of ordinary skill in the art in 1995, therefore, would not have pursued the path of a product that caused irritation or burning?"

And your answer was: "Correct."

A. **Yes.**

Q. **Were you here in the courtroom when Dr. MacKay was testifying, to hear that Flonase also causes nasal irritation?**

A. **I believe he said that, yes.**

Q. **And he also testified that Flonase causes burning?**

A. **Okay.**

Q. **Now we have the Nasacort AQ package insert. And we can look at the adverse effects here.**

Among the adverse effects, we have, to the

right, the little table, increasing cough, epistaxis and pharyngitis. Irritation is not one of the reported adverse effects. Correct?

A. Let me read it, please.

It doesn't seem to be listed, no.

Q. Thank you. So it is not one of the reported adverse effects in the package insert?

A. In the package insert, that's true.

Q. Now, you testified some about the Setipane article in relation to your obviousness determination, and said that it didn't have a list of the ingredients, but it might lead someone of ordinary skill in the art in a certain direction.

But the Setipane article would not enable a person of ordinary skill in the art in 1995 to make the TAA aqueous nasal spray. Correct?

A. Not completely by itself, no.

Q. And the Kobiyashi article, the other one that you read, would not enable a person of ordinary skill in the art in 1995 to make the TAA aqueous nasal spray. Correct?

A. Same answer, yes.

Q. You testified that the issue of CFCs was well-known to people of ordinary skill in the art. Right?

A. Yes.

Q. And one of the things you relied upon was Defendant's Exhibit 33, which we have already established was an

internal RPR document that a person of ordinary skill in the art would not have known about?

A. **Which one was that?**

Q. **I am sorry? That was the rationale document.**

A. **Okay.**

Q. **Correct. It would not have been known to a person of ordinary skill in the art?**

A. **That's true.**

Q. **And the other document that you specifically relied upon was a patent application, WO9214473. It is Defendant's Exhibit 13. Right?**

A. **Yes.**

Q. **But that was a patent application from Switzerland. Right?**

A. **Yes. I believe it was.**

Q. **And --**

A. **Yes.**

Q. **-- CFC's were something that were being phased out in other parts of the world, but there wasn't a big push to phase out CFC's in the eighties an nineties, at least up to 1996, in the United States, was there?**

A. **As someone who was formulating in that time frame, it was known that CFCs were going to be removed from the market. And the issue here really from a corporate formulator's point of view, I should say from a corporate**

development point of view, is you have to anticipate what's going to happen in the market. You know, you can't say, okay, I am going to -- CFCs are going off the market tomorrow and I am going to have a -- you have to have a product ready to go and switch your people or your patients over to that product.

You know, for example, you saw the rationale memos internally were 1991. The patent got filed in, what, '95, and I have forgotten the date where the product, you know --

Q. Was there a big push in the 80s and early 90s to get rid of CFCs in pharmaceuticals in the United States?

A. It depends on how you define "big push."

Q. Well, as you define "big push."

A. Well, I said it. Therefore, I must mean it.

Q. Well, if I could have you turn to your deposition again.

In fact, was there any push to do it in the United States? You know what, I won't define it as "big push." Was there any push to formulate outside CFCs in the United States in the 1980s and early 1990s?

A. Well, I think the witness that there was a push or there was a knowledge that there was going to be a necessity to go from aerosols was the fact that Beconase and Vancenase had done it and actually reformulated their products as an

aqueous suspension and had taken over 60 percent of the market.

Q. Now, that is not something you put in your report, that Beconase and Vancenase had done it so other people would want to do it. Right?

A. No, I think you can't take -- what you are doing is you are taking little bits of pieces of knowledge and trying to -- you know, a person of ordinary skill in the art has lots of knowledge and lots of information from many different places, his education, his experience, the literature that he reads every day. All of that goes into the decisions that a person would make and all of the knowledge that would be used when they're looking at formulating a product.

Q. So that is something that might have been known to a person of ordinary skill in the art but it wouldn't be something you put in your report as part of your opinion?

A. I guess it was assumed something. I was easily knew that and I easily read it.

Q. You talked about EDTA to some degree here and you talked about it as part of a preservative system but really the primary application of EDTA in pharmaceutical formulations like this one is as a chelating agent. Is that correct?

A. That's true.

Q. **And you have no reason to believe that phenylethyl alcohol performing the function of a chelating agent?**

A. **No.**

Q. **And I believe you said this on direct but I just want to make it absolutely clear. Every nasal preparation that you cited uses EDTA in a solution, not a suspension?**

A. **That's true.**

Q. **In fact, to your knowledge, Nasacort AQ was the first nasal spray suspension that used a chelating agent?**

A. **Well, I can't say that. It used the -- yes, let's use the EDTA.**

Q. **Let's use the chelating agent. To your knowledge, at the time you formed your opinions, was there any nasal suspension preparation, as of July 1995, that used a chelating agent?**

A. **No, I think you're right. I stand corrected.**

Q. **I want to switch back to phenylethyl alcohol. And phenylethyl alcohol is in Beconase AQ and Vancenase AQ and Flonase?**

A. **Right.**

Q. **Now, a person of ordinary skill in the art in 1995, he or she or they would have reason to believe that the preservative system of benzalkonium chloride and phenylethyl alcohol would potentially increase drug absorption over the same formulation without that preservative system?**

A. **Yes, I think, I believe that was in the literature.**
Q. **In fact, it was in your literature. You wrote that.**
A. **True.**
Q. **And if you would turn, in the In Vivo Evaluation of Spray Formulation of Human Insulin For Nasal Delivery article, to page 102.**

And as part of what you did in relation to this article, you studied the effect of the phenylethyl alcohol, benzalkonium chloride preservative system on nasal absorption of insulin. Right?
A. **Yes.**
Q. **And it was in an MCC spray formulation; right?**
A. **Yes.**
Q. **And in that formulation, the preservatives provided a higher absorption of insulin when compared to the same formulation without the preservatives. Right?**
A. **Correct.**
Q. **And you suggested that the greater absorption of insulin seen with these preservatives may be due to their surfactant nature as well as their ciliotoxicity, which allows insulin longer residence in the nasal cavity due to reduced mucociliary clearance. Do you see that?**
A. **Yes.**
Q. **I want to focus for a second on the ciliotoxicity. That means it kills or harms cilia; right?**

A. **What it actually does is it reduces the peak frequency.**

Q. **Kind of narcotizes?**

A. **Yes, I guess that is a way to put it.**

Q. **And that is something you see with phenylethyl alcohol and benzalkonium chloride together but you don't see it with EDTA and benzalkonium chloride. Right?**

A. **I don't know.**

Q. **You have no knowledge on the benzalkonium chloride/EDTA combination?**

A. **I know you would see it with benzalkonium chloride by itself. It was well known. I don't know if you would know, if you would see it with the combination of EDTA plus benzalkonium chloride.**

Q. **So that is just something you don't know?**

A. **That is right, I have never see the data.**

Q. **And a person of ordinary skill in the art wouldn't know it either?**

A. **Well, not because I don't know. Maybe they would look in the literature.**

Q. **You know of no literature and, in forming your obviousness opinion, you found no literature that would suggest that the combination of EDTA and benzalkonium chloride led to this narcotization of the cilia?**

A. **That's true.**

Q. **It's also possible that the ciliotoxicity is due to the benefits of phenylethyl alcohol, isn't it?**

A. **I don't know. It's possible that it contributed but, again, we didn't partition up the two compounds.**

Q. **If I could have you look back at the Handbook of Pharmaceutical Excipients.**

THE COURT: Counsel, how much more do you have? Because we probably should do a break at some time.

MR. RICH: Well, it depends on how he answers. Probably five to ten minutes, Your Honor.

THE COURT: Let's take a break.

(Recess taken.)

THE COURT: Please be seated.

We'll resume with counsel's cross.

MR. RICH: Just a few more questions.

THE COURT: All right.

BY MR. RICH:

Q. **We were talking about the preservative system of phenylethyl alcohol and benzalkonium chloride and the ciliotoxicity effect of that combination. Right?**

A. **Yes.**

Q. **And I asked you whether it was likely that phenylethyl alcohol is the primary ciliotoxic ingredient?**

A. **Correct.**

Q. **Do you believe that phenylethyl alcohol is the primary**

ciliotoxic ingredient?
A. I don't know, to be honest with you. I know benzalkonium chloride is traditionally on the list of ciliotoxic and, just, it's possible but I, to be perfectly honest, I really don't know.
Q. We looked at this before. The Handbook of Pharmaceutical Excipients.
A. Yes.
Q. Let's look at the entry for phenylethyl alcohol in the description section which says, it has a burning taste which irritates and then anesthetizes mucous membranes. Do you see that?
A. Yes.
Q. And that could be the ciliotoxic effect?
A. Possibly, I guess.
Q. And you have no reason to believe that the Handbook of Pharmaceutical Excipients is wrong on this point, do you?
A. No, I don't think I want to say anything about the Handbook of Pharmaceutical Excipients.
Q. And you are not qualified to make the decision whether Flonase would be odorless if it caused a burning sensation?
A. True.

MR. RICH: Thank you.

Your Honor, I have nothing further.

THE COURT: Mr. Hurst, you may redirect.

MR. HURST: Very briefly, Your Honor.

REDIRECT EXAMINATION

BY MR. HURST:

Q. **Dr. Needham, when conducting your analysis about what the prior art disclosed and taught to one of ordinary skill in the art, you said during cross-examination that you didn't focus on the specific viscosity values in the Court's Markman ruling. Do you remember saying that?**

A. **Yes.**

Q. **Did we, at Barr Laboratories, have a different expert determine experimentally whether the prior art Flonase solution matched those viscosity values?**

A. **Yes.**

Q. **Who would that be?**

A. **Dr. Klingenberg.**

MR. HURST: Thank you. I have no further questions.

THE COURT: All right. Thank you, doctor. You are excused.

THE WITNESS: Thank you, sir.

THE COURT: All right. Mr. Hurst, your next witness.

MR. HURST: We are resting our case subject to the admission of dep. designations that I understand by agreement we're giving you at the end the case. So we're

resting our case.

THE COURT: All right.

MR. HURST: Thank you.

THE COURT: Is there going to be a rebuttal case?

MR. BERGHOFF: Yes, there will be a rebuttal case. First, Your Honor -- and this is at your pleasure. Would you like a brief oral Rule 52 motion?

THE COURT: You can go right ahead.

MR. BERGHOFF: I'm going to ask my partner, Aaron Barkoff to deliver that to Your Honor. Thank you.

THE COURT: Okay.

MR. BARKOFF: Good afternoon, Your Honor.

THE COURT: Good afternoon.

MR. BARKOFF: Plaintiffs request a judgment under Rule 52 that Barr has failed to prove invalidity by clear and convincing evidence. I have three brief points.

THE COURT: Okay.

MR. BARKOFF: First, Barr has failed to prove that the Phase III clinical trials were a public use. The parties agree that a public use is a use of the claimed invention by a person other than the inventor who's under no limitation, restriction or obligation of secrecy to the inventor.

Barr has not offered any evidence that either

the principal investigators or the patients who participated in the clinical trials were under no limitation, restriction or obligation of secrecy, much less clear and convincing evidence of that.

Barr has focused its arguments on the patients who enrolled in the clinical trials; arguing that because they did not sign a confidentiality agreement, that made their use of the claimed invention a public use. But the case law clearly establishes that that fact is not dispositive of public use because patients may be under other limitations or restrictions. Barr has simply failed to show there was any use of the invention by a person who was under no limitation or restriction.

Second, Barr's failed to prove that the claims are not enabled. Barr has not shown, by clear and convincing evidence, that the specification of the patents in suit does not enable one of ordinary skill in the art to make and use the claimed invention. Dr. Donovan, yesterday, admitted if Dr. Berridge's PET results are true, then the claims are enabled. Barr has failed to prove by clear and convincing evidence that Nasacort AQ does not deposit in the frontal sinus. In fact, the weight of the evidence shows the opposite.

Third, Barr has failed to prove that the invention would not have been obvious. Here, all the prior

art products that Barr relies on for obviousness lack at least two key features recited in the asserted claims. One, odorlessness and, two, a particular viscosity profile. None of the prior art products are odorless. None have the specific velocity profile of Nasacort AQ. In addition, Barr has not shown there was a reason to combine the prior art products and create a product that has those properties. Therefore, Barr has failed to establish obviousness by clear and convincing evidence.

For those reasons, Your Honor, plaintiffs move for a judgment under Rule 52 that Barr has failed to prove invalidity.

THE COURT: Thank you, counsel.

Are you going to respond?

MR. HURST: If you would like me to, yes.

THE COURT: Yes.

MR. HURST: Under public use, Your Honor, the law is pretty clear. If there is a nonconfidential use of the claimed invention, it is in fact a prior public use. In the record, Settipane, Kobayashi demonstrate that 600 people used the claimed invention in the prior art, the exact claimed invention, Nasacort AQ.

In the record, that they did it with no confidentiality agreement, is DX-316, Paragraph 63. The Simpson deposition transcript where this is admitted -- it's

not even a contested fact, Your Honor -- at 182, 9 through 22, which is one of the deposition designations.

With respect to enablement, you heard from Dr. Donovan who has been in this business for 20 years who said that reading this patent application, it is Nasal Spray 101. It doesn't teach you anything more than the prior art with respect to how to get to the frontal sinus.

Counsel argued that the weight of the evidence shows that the nasal spray does in fact get to the frontal sinus. The point I would like to focus on is Dr. MacKay's graphic of an actual frontal sinus, that long thin tube. The notion that a spray would get up that long thin tube without touching a wall, that alone seems to us to prove the opposite fairly definitively in our view.

And with respect to obviousness, you have just heard from Dr. Needham who has been in this business for 40 years. And what he has demonstrated is that not only was this Nasacort formulation obvious, it was in fact a copy of the prior art; not only one prior art formulation but three prior art formulations.

And so for those reasons, Your Honor, we would oppose the motion. Thank you.

THE COURT: The Court will deny the motion for at least a number of the reasons just articulated by Mr. Hurst. There are many others. I have no difficulty

denying the motion, with respect, counsel.

MR. BERGHOFF: Before we call our first rebuttal witness.

THE COURT: Yes.

MR. BERGHOFF: I just wanted to review with Your Honor scheduling. It would be my preference to call Mr. Simpson first -- it would make the most logical sense. He is a brief witness -- followed by Dr. Kaliner. Dr. Kaliner has to be walking out the door at 5:30. I know Your Honor can't help me with the times. I think it's going to work out but if Your Honor were unable to hold court in session until 5:30, then that would make my decision for me.

THE COURT: It's a long day, counsel, particularly for my court reporters. It's a long day and you have to be sensitive to the fact there is only so much the jurist can absorb at any given time. So I would suggest that you make sure you can get us out here at a reasonable time. That is the guideline I'm going to give you.

MR. BERGHOFF: My call is clear. We will be calling Dr. Kaliner as our first rebuttal witness.

THE COURT: Okay.

(DR. MICHAEL A. KALINER, previously sworn, retakes the witness stand.)

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THE DEPUTY CLERK: Dr. Kaliner, you are reminded

that you are still under oath.

MR. GRACEY: Your Honor, there is one issue before we get started with Dr. Kaliner. Plaintiffs informed us this morning that they wanted to introduce a new exhibit that hadn't been disclosed in the pretrial order. It hadn't been on any exhibit list. We think it's inappropriate and hereby object to the exhibit; and I believe they want to use it with this witness.

THE COURT: With this witness?

MR. RICH: That is correct.

THE COURT: Do you want to tell me what it is, the reasons that you have just announced that you are objecting?

MR. GRACEY: Would you like me to explain what it is?

THE COURT: Well, it's your objection, so ...

MR. GRACEY: Yes. Okay. What it is, Your Honor, is it appears to be a nebulizer, some kind of document related to a nebulizer, not a nasal spray. And it's a printout from a -- it looks to be like a website of some sort or a press release dated June 4th, 2007. So it's been around almost a year. Plaintiffs have known about our case. We've known about each other's cases for years. If they wanted to use it, they clearly had a year to put it on the exhibit list.

THE COURT: What is your response?

MR. RICH: Your Honor, if I might approach and give the Court a copy?

THE COURT: Yes.

(Document passed forward.)

MR. RICH: Your Honor, this is an issue prompted entirely by the testimony yesterday of Dr. Donovan. And it will show the Court -- hopefully assist the Court, I should say -- that the weight of the evidence shows that products can get to the frontal sinus.

Dr. Donovan testified to a question: Now, in all your years of experience, in this area of study, have you ever heard, have you ever heard of a nasal spray that reliably reached any of sinuses, much less the frontal sinus?

And Dr. Donovan responded: No, I haven't.

Now, if permitted to testify, Dr. Kaliner will testify that this is an accepted therapy. It's a nasal spray. In fact, an intranasal --

THE COURT: But this whole new area of inquiry, counsel, and this has been an issue in this case from Day One.

MR. RICH: Your Honor, it's a different question from what was has been in the case from Day One. It has been a question whether Nasacort would reach it, but the

credibility of Dr. Donovan I would submit is diminished by the fact that there are nasal sprays that do reach the frontal sinus and are used as treatments for sinusitis.

THE COURT: I might let you make those inquiries but I don't believe it fair or kosher to permit the use of this document to do that.

MR. RICH: Fair enough.

THE COURT: Your reaction.

MR. GRACEY: Yes. My reaction, judge, is he is mischaracterizing the document. It's not a nasal spray and you will not see the words "frontal sinus."

THE COURT: Anywhere on the document. I'm going to give this back to you. Okay?

MR. RICH: Sure.

(Document passed back.)

MR. RICH: Thank you, Your Honor.

THE COURT: Okay. So I'm going to, for the record, sustain that objection.

MR. GRACEY: Thank you.

MR. RICH: Thank you, Your Honor.

Your Honor, if I might approach?

THE COURT: You may.

(Binders passed forward.)

DIRECT EXAMINATION

BY MR. RICH:

Q. **Dr. Kaliner, I'd like to start by talking about clinical trials. Can you refresh our memories about your experience with clinical trials?**

A. **The Institute for Asthma and Allergy of which I'm the founder is heavily invested in clinical trials. And we do somewhere between 15 and 30 per year. We've probably done 500.**

Q. **And have you been involved in those clinical trials?**

A. **I have been involved in the trials. I've done, I've administered the trials. I have designed trials. I've critiqued trials. I've reviewed the results of trials. I mean I have done everything you can do at trials.**

Q. **What phase trials are those that you are speaking of?**

A. **We predominantly do Phase III trials and occasionally Phase IV trials.**

Q. **Can you tell me what Phase III trials are?**

A. **Phase III trials are mandated by the FDA to bring a product to licensure in the United States. So the FDA requires that companies take a product that they're interested in and do a placebo-controlled, balanced trial over a certain period of time with a certain number of patients and have a set end point that is predetermined that shows clinical significance and also demonstrates safety. So these are FDA required trials before any product can be licensed in the United States.**

Q. **And when you say "can be licensed in the United States," what effect does that have on the distribution of the drug in the United States?**

A. **Well, a product cannot be legally sold in the United States as an ethical pharmaceutical without FDA approval. So it is an absolute prerequisite before any product can be sold.**

Q. **Are there any ethical requirements regarding what information must be given to patients in Phase III trials?**

A. **Yes. There is a detailed quite lengthy informed consent document that is constructed, reviewed and approved by the FDA that has to have all the essential ingredients of the trial outlined in very simple language, because most of our volunteers are not well educated. And so in very simple language, we have to spell out: What is the active ingredient? What are the possible risks? What are the possible benefits? All the details of the trial itself. And we need to go over that with the patient; and they have to sign it prior to any inclusion in the trial.**

Q. **And are there any ethical requirements regarding how patients can use information they receive in a clinical trial in relation to their treatment by other caregivers?**

A. **Well, I mean patients have to know what they're on in the trial. We do do things in some of our experiments that involve unusual experiments. The exposure to medicines that**

could conceivably have side effects or, God forbid, one of the patients got sick and they have to go and be signed in an emergency room or what have you. They have to know what they're on. They have been to be informed what they're taking, and why, and what are the possible risks they're entailing.

Q. Now, you testified that most of your volunteers are not especially well educated; and we heard in the opening, as far as Aventis knew, these were pharmaceutical formulators or their brothers or sisters or parents were pharmaceutical formulators. Who are the participants in clinical trials for allergies?

A. In a setting like mine, where we take care of literally tense of thousands of patients, we recruit largely within our patient population. And so we have paints that we know, with whom we have a very long relationship. We take care of them clinically. We invite them to participate in a trial into which they fit because they have certain prerequisites. They then do the trial; and we continue to take care of those patients. So we have a very long and, you know, knowledgeable relationship of these patients before we involve them in a trial. So it would be difficult for me to imagine that we have very much pharmacists or formulators that come to our trials.

Q. And in these allergy trials, how much of a drug do the

patients receive at a time?

A. Well, if it's a spray like what is in question here, the patients get just enough spray to last them for the weeks of the trial. So depending on the two trials we're talking about, either two weeks or three weeks, and they are seen -- in the three-week trial, they are seen in the interim. And so you are giving them a milliliter or two milliliters. Each spray is 100 microliters, and you are giving them just enough spray to last during the duration of the trial. So it's a few milliliters. So a teaspoon is five milliliters. So that puts it in perspective. It's a few milliliters less than a teaspoonful of a reagent in most of these trials.

Q. And you said these are placebo-controlled trials, the Phase III trials. What does that mean in terms of what a patient would know regarding what they would receive?

A. Well, the patient would be informed that they could be either getting an active product or placebo but they would not know which one they were getting. And, in fact, we do not know which one they're getting. These are called double blinds. So we're blinded, the patient is blinded, and only the contract research organization that regulates the trial has any idea who is getting what. And so there is a 50 percent chance the patient will be getting a matched placebo.

Q. **Do all drugs succeed in proving safety and efficacy in Phase III trials?**

A. **By no means do all drugs succeed in Phase III trials. That is why you do trials. You formulate a product, and you hope that it will do what you want it to do. But there is only one way in the United States to find out whether it does it, and that is it has to be a Phase III clinical trial.**

Q. **Do you have any perception -- actually, if you could turn in your binder to Exhibit 420. And I believe we have represented some of the information. Can you tell me what this article deals with?**

A. **This is an analysis of a clinical trials. They took 280 trials and looked at the breakdown of trials that have succeeded and those that have failed, trying to analyze why a substantial number of the trials failed.**

Q. **And I think if we turn to the last -- oh, there we go.**

MR. GRACEY: Your Honor?

THE COURT: Yes, sir.

MR. GRACEY: Just briefly, I'm not sure where counsel is going with this but in the entirety of Dr. Kaliner's report, there is no discussion of any failures. So if he going into secondary consideration, I would object for the record.

THE COURT: Okay.

MR. RICH: Your Honor, if I could just beg the Court's indulgence to get the paragraph number?

THE COURT: Sure.

MR. RICH: This specific document is referenced in his report at Paragraph 40, Page 19. I could hand it up, Your Honor, if you would like.

MR. GRACEY: I just wanted to make sure to note if he goes into failures of others, that that is not disclosed. To talk about this, I don't have any problem.

MR. RICH: Your Honor, I think we'll go to the same -- first, I do believe that I will be talking about failure of others. And I do believe that that is addressed expressly in his report in Paragraph 40. There are specific failures of Phase III trials in intranasal sprays that are addressed in that paragraph.

THE COURT: Counsel.

MR. GRACEY: Your Honor, I believe, like I said, I have no problem with Dr. Kaliner talking about Phase III trials in general, but if he is going to translate that into secondary considerations as it regards Nasacort AQ, I would object.

THE COURT: Do you understand the objection?

MR. RICH: I do understand the distinction. And I'm suggesting that this is discussing the nature of Phase III trials and, in fact, they are experimental.

THE COURT: Sure. Okay. That's fine. I don't think there is an objection to that.

MR. GRACEY: I have no problem.

MR. RICH: I apologize for my misunderstanding.

THE COURT: No problem.

BY MR. RICH:

Q. **Turning back to the article. It says here that only 58 percent of the trials are successful, which means that about 42 percent, if I got my math right, failed. Is this consistent with your understanding of Phase III clinical trials?**

A. **Yes. More or less, right. That there are a substantial risk of failure; and I have seen many.**

Q. **Can you tell me some specific examples of failure that you saw?**

A. **I think it was mentioned earlier. We talked about, I think it came up, this tipredane, a steroid that was being brought along as what was called a soft steroid; that is, a steroid that could be used for asthma and rhinitis but have fewer side effects. And, in fact, it just simply failed, had no efficacy above placebo. This is work that was done, it was by a company that made a good asthma medication and they were trying to find a successor. And the product simply failed. It did not work at all despite everything in Phase I and II, and all the information would have suggested**

it would have been effective.
Q. We're looking at now Plaintiffs' Trial Exhibit 421. And this is a press release. Is that what you are talking about where it says that the tipredane had simply not been effective in clinical trials?
A. Correct.
Q. And you said tipredane had been mentioned. Are you talking about Dr. Needham's discussion of a patent application that he relied upon in relation to his obviousness opinion?
A. That is correct. That was surprising, too.
Q. Do you know of any other nasal sprays that have failed in Phase III trials?
A. Let me give you three examples. One is -- the first two are products that I actually developed the protocol for and studied with a small company that -- and it was doxepin nasal spray. So there was every reason to think doxepin would work. It's an antihistamine known as Sinequan in the 80s as a tranquilizer. It's a very, very good antihistamine. And it's on the market as a salve which you put on the skin for itching and it's very effective. It's very good. It's good orally. It's good as a topical. It's a very potent product; and we thought for sure it would work as a nasal spray antihistamine. In fact, it had no activity whatsoever above placebo.

So then there was work that was being done in Europe on a product called Capsaicin. Capsaicin is the essence of hot pepper. That is what makes hot pepper tasty and spicy. It was thought in Europe that if you sprayed it in the nose, it could be useful for nonallergic rhinitis. And so we did that project in our office, in our lab; again with another company; and it was unacceptable in that, as you might imagine, it hurt too much. We could not formulate a product that the patients could tolerate so side effects limited that product.

And the third is totally surprising. And that is that epinastine, which is sold as Elestat. It's on the market. We have a sizeable number of patients using it as an eyedrop antihistamine. Eyedrops should work in the nose. There are continuous mucus membrane, as has been pointed out in my other testimony this week. That the nose and the eyes are very similar to each other. So one would fully anticipate that an eyedrop antihistamine would work and it failed. It was withdrawn from market about a month or six weeks ago because of total failure at trial. This is very current.

Nonetheless, you can never assume that a product is going to work until you do clinical trials and it works.

Q. I'd like to turn specifically then to the clinical trials that Rhone Poulenc Rorer ran that have been

discussed, the phase III clinical trial. And you reached an opinion, didn't you, as to whether these clinical trials were experimental or public use?

A. **Well, they were experimental.**

Q. **If we could look at the factors? That I think we prepared a slide of factors. Were these the considerations that you applied in determining whether it was experimental use?**

A. **Yes.**

Q. **And I guess I can read them just as well as you can but:**

The necessity for public testing.

The amount of control over the experiment retained by the inventor.

The nature of the invention.

The length of the test period.

Whether payment was made.

Whether there was a secrecy obligation.

Whether records of the experiment were kept.

Who conducted the experiment.

The degree of commercial exploitation during testing.

Whether the invention reasonably required evaluation under actual conditions of use.

Whether testing was systematically performed.

Whether the inventor continually monitored the invention during testing.

And the nature of the contacts made with potential customers.

MR. GRACEY: Your Honor, if I may. I will object on relevance grounds. The reduction to practice date has been set by plaintiffs as of 1992. So as a matter of black-letter law, experimental use is not in the case.

MR. RICH: Having done further research from the last time we were before Your Honor, first of all, we believe that the black-letter law is not so black. It's gray at best. And we believe, we are hoping that Your Honor finds that it's experimental use.

Second, we believe it certainly is still relevant to the issues in this case.

THE COURT: Go ahead.

BY MR. RICH:

Q. If we could start with the first one. The necessity for public testing. Actually, before we get into the necessity for public testing...

Was there something unusual about the way this study was designed in your mind with regard to a Phase 3 clinical trial for a nasal allergy product?

A. No.

Q. What was the interaction between Rhone-Poulenc Rorer

and the doctors?
A. Well, what happens with these clinical trials is that Rhone-Poulenc Rorer will approach physicians, and ask them, are they able to do the study. Are they interested in the study and are they capable of recruiting patients adequately into the trial? And can they follow the rules and law that regulate clinical trials?
Q. What happens next, if they agree that they can follow the rules and laws that govern the clinical trials?
A. There is generally a meeting where we get together, all the investigators get together, and discuss the details of the trial. It's usually a one- or two- or three-day meeting, where all the details are reviewed and hashed out to make sure that there is no defects in the design. So it's a very interactive time. Then the clinical trial is finalized and has to be approved by the FDA and then put in place.

Rhone-Poulenc Rorer has something to do with it, but they also have a CRO that is usually involved. So there is a contract research organization that plays a role between RPR and the physicians. So there is direct contact with RPR. Once the product is started, it's done by a CRO.
Q. When you say the clinical trial is finalized, is there a protocol developed?
A. Yes, there is a very detailed protocol that has every

detail of the study. And there is also the creation of a series of papers, what we call source documents. They go through every single step of the study, it's documented, so that there is a checklist in a required form that gets filled out for every single detail of the study for every patient.

Q. Does a doctor undertake any obligations towards Rhone-Poulenc Rorer -- did the doctors in this case undertake any obligations with regard to Rhone-Poulenc Rorer in these clinical trials?

A. I don't know what you mean.

Q. In terms of confidentiality?

A. Absolutely. Yes. What happens is that we are sworn to a confidentiality agreement, so we cannot talk about anything to do with this trial during the trial or thereafter. You have to be free from that obligation. That's generally when the product comes on the market.

Q. If I could have you turn to Plaintiffs' Exhibit 425, that same book in front of you.

Especially the second-to-last page, Page 31, there is a signature line, where you were the principal investigator. What does a signature on that line represent?

A. It means that the investigator has read and agreed to everything in the document and has sworn that he will not diverge information about the study.

Q. **Turning back to Page 29 of this document, the use of information and publication, is this the confidentiality obligation that the investigator undertakes?**

A. **It is.**

Q. **And undertook in these clinical trials?**

A. **Yes. I have seen documentation of the signed informed consent of confidentiality agreements with each of the investigators.**

Q. **Do the subjects of the clinical trials, did the patients in this case receive any information?**

A. **Yes, they have an informed consent. As I said before, that's quite detailed and so they knew the name of the active ingredient, they knew that a similar -- that another product was on the market, with the same ingredient.**

Q. **Did they know any of the excipients in the product?**

A. **No, of course not.**

Q. **And what was done with the samples after they were given to the patients for use?**

A. **Well, the patients were instructed in their use. It was two sprays each nostril once a day, depending on the study, and some of them went back to one spray each nostril once a day in one of the studies.**

The bottles were collected periodically through the study in order to account for the volume of spray to be sure that patients were being compliant with the study.

So the drugs were given out and then collected as we always do and returned to the company and measured.

Q. **Is that something required by federal law, that you collect the bottles?**

A. **It's done in every study.**

Q. **From Page 23: All disposition of clinical supplies must be recorded and accounted for as required by federal law at the completion of the study.**

Did the patients keep any records of their use of this drug?

A. **Well, they had a diary. There are diaries that they fill out that record symptoms. So they had diaries that they were recording. Those diaries were collected as well during the course of the study.**

Q. **When you say they are collected, who collected the diaries from them?**

A. **The physician or his designate. We have a number of clinical study coordinators with whom we work. And they are actually directly in contact with the studies, the patients who are studied.**

Q. **There is a line for the signature of the clinical trial coordinator in the investigator's brochures?**

A. **Correct.**

Q. **So they undertake the same confidentiality application?**

A. **They do. They are well-trained. They have to pass a test. So they are well-regulated.**

Q. **After the doctors collect the data, what is done with the data?**

A. **Well, during the course of the study, we are very, very, very carefully regulated. So the CRO visits our office on a periodic basis, sometimes depending on the studies many more times than you want them to, but they are there frequently, at least every week or so. They review all the documents. It's not like you are ever left on your own. You are never left on your own. The clinical study coordinators are supervising every step of the way to make sure all the documentation is accurate and filled in correctly and interacts with our study coordinators and with the physician. So there is a very, very close interaction going on on a constant basis with the CRO.**

Q. **To be clear, the doctors in these studies, did they ever know which samples had active ingredients and which had placebo?**

A. **No. These are double-blind placebo controls, so nobody knows, nobody actively involved in the experiment except for the CRO might know. But we don't know.**

Q. **And that would include patients, too?**

A. **That's correct. It involves the physician, the study coordinator, and the patient would not know.**

Q. **Now, in these trials, were the patients kept confined?**
A. **No. The FDA actually requires us in these studies to let the patients be exposed to the same conditions that cause the disease. So if you had patients quarantined or someplace, they wouldn't be exposed to the allergins to which they are being studied.**

So the studies are done seasonally, so that patients are exposed to an allergin that is in the air and they are asked to do their usual life except for taking part in the study.

It is an ambient study under natural conditions. That is required by the FDA.
Q. **After the CRO collected all the data, what did it do with that data?**
A. **It analyzes it, puts it together, and goes, interacts with Rhone-Poulenc Rorer at the time. We have nothing to do with it. Once the data has been collected, our job is over, except for final reports that take place, to make sure all the paperwork is accurate.**
Q. **Now, in your binder you have Plaintiffs' Trial Exhibit 192, which looks to be 350 pages.**
A. **Right.**
Q. **I apologize to the environment.**

Can you tell me what that is?
A. **This is the protocol. And, so, you are looking at the**

details of the protocol. It's the background and the details of what we have to do.

Q. **Going back to the factors that we were talking about, in terms of experimental use, the first one is the necessity of public testing. But if you could tell me, just to clarify, whether you think that public testing was necessary in this situation?**

A. **Well, it is the only way to get a drug on the market in the United States. So it's absolutely 100-percent required.**

Q. **And in terms of determining the efficacy or safety of the drug, was public testing necessary?**

A. **Absolutely. It's the only way you can determine safety and efficacy.**

Q. **The second factor is the amount of control over the experiment retained by the inventor. What control did RPR maintain over this trial?**

A. **Well, they were intensely involved in the creation of the protocol. That is their protocol. But once the protocol is in place, it is then done by -- it's automatic. The CRO and myself and the coordinator do everything as prescribed.**

So we had no contact with RPR whatsoever at that point.

Q. **But after the experiment was over, at the conclusion**

of the experiment, who maintained control of the data?
A. RPR and the CRO would work with the data together. But we would not.
Q. Who selected the CRO?
A. RPR would select the CRO.
Q. The third factor is the nature of the invention. How do you believe the nature of the invention affected whether this was experimental use or public use?
A. I am not sure I understand the question.
Q. Was there anything about the nature of this invention, the TAA nasal spray, that would affect whether you would perform an experiment that required interaction with the public?
A. Well, you could not tell that the nasal aqueous preparation of TAA would work. I mean, as I said before, I would have bet anything that Elestat would have worked as a nasal spray. There is absolutely no reason why Elestat given into the nose shouldn't have been quite effective. But it wasn't.

So by nature of the way that studies have to be done, TAA had to be studied.
Q. The next factor is the length of the test period. How long were these trials?
A. That's really prescribed. At the time of these studies, seasonal allergic rhinitis was a two-week study,

one-week run, that's a total of three. The PAR studies, perennial allergic rhinitis by requirement of the FDA, was a four-week study. That is just laid out by the FDA.

Q. The fifth factor is whether payments were made. Do you know if there were any payments made at these trials?

A. I can tell you what we had at our center. We reimburse patients on the basis of time involved. We give them a basis, it's about 20 to 25 dollars an hour for time involved in the experiment. But I do not believe that all the sites in this particular study paid their volunteers. Some of them were purely volunteer participants who got no payment whatsoever. But I think that the majority probably got some payment. But these -- you are talking about a few hundred dollars maximum.

Q. Did the patients pay anything for the drug that they were getting?

A. Oh, of course, not.

Q. Whether there was a secrecy obligation, now, I believe you talked about something related to that?

A. Yes. I mean, there was a requirement for confidentiality.

Q. Were the records of experiments kept?

A. Hundreds of pages per patient.

Q. Who conducted the experiment?

A. Well, as I said before, it's regulated by a CRO, but

conducted by the physician and his coordinator on site.

Q. The degree of commercial exploitation during testing. Was there commercial exploitation during testing?

A. Tell me what you mean by commercial exploitation.

Q. Did they sell the drug?

A. Of course not. First of all, the drug is not for sale. The patients only knew the active ingredient. There was no contact with the company whatsoever.

Q. Was Rhone-Poulenc Rorer marketing the drug during this time?

A. To the patients?

Q. To anyone.

A. Well, they were marketing the aerosol product. But not this particular product. So the Nasacort AQ was certainly not commercially available.

Q. Do you believe the invention reasonably required evaluation under actual conditions of use?

A. It was the only way you can tell whether the product would work or not, and it's required by the FDA.

Q. Do you believe the testing was systematically performed?

A. Yes, it was absolutely rigorously performed in a systematic fashion.

Q. Was the test continually monitored, the invention continually monitored during testing?

A. **As I said, each of these studies is scrupulously supervised.**

Q. **And what contacts did RPR, if any, have with potential customers, the subjects in the trials?**

A. **I can say absolutely none.**

Q. **So do you have -- I know I asked you before. But your conclusion with regard to whether there was public use or experimental use was?**

A. **Well, there is no question it was experimental use.**

Q. **I would like to change topics to --**

MR. GRACEY: Your Honor, I move to strike.

THE COURT: It seems to me that is a question of law.

MR. RICH: It's based on facts.

THE COURT: It's a question of law.

MR. RICH: I will defer to Your Honor.

THE COURT: There may be facts that underpin my ultimate determination. But I get to decide whether it's public or experimental use. That's the point.

MR. RICH: You get to decide everything.

BY MR. RICH:

Q. **I would like to move to the topic of certain potency issues, and ask you, are you familiar with something called the MacKenzie Skin Blanching Test?**

MR. GRACEY: Your Honor, may we approach?

THE COURT: Yes.

(The following took place at sidebar.)

MR. GRACEY: You may recall that Dr. Meltzer was up, during the case-in-chief he began talking about potency. I raised an objection saying I was concerned whether there was going to be their obviousness case. I also recall during the pretrial conference, actually, about the overlap of experts. We have Dr. Meltzer and Dr. Kaliner. The exact same demonstratives that they gave us last night from Dr. Kaliner they gave it for Meltzer. My supposition is they are going to do it with Meltzer tomorrow.

MR. RICH: We will not do it with Meltzer tomorrow.

MR. GRACEY: While we are here, it is the same issue with regard to patient preference studies. I don't mind one of them. I just don't like a lot.

THE COURT: I don't, either.

MR. RICH: Your Honor, we are not going into patient preference studies with Dr. Kaliner.

(End of sidebar conference.)

BY MR. RICH:

Q. **Are you familiar with the MacKenzie Skin Blanching test?**

A. **Yes, I am.**

Q. **How does that work?**

A. **One of the properties of corticosteroids is they are vasoconstrictors, and that is a direct and immediate response. It turns out if you put a steroid on your scan, it blanches the blood vessels in the skin, so it's a blanching assay. It turns out, by luck, that there is a relationship between the strength of skin blanching and the potency of steroids. So this is an easy screening procedure to get an idea of how potent the steroid is. It is done as a routine for all steroids.**

Q. **Do you know whether all steroids have the same potency in the MacKenzie Skin Blanching test?**

A. **Well, no, they don't. And that's where there is a hierarchy, if you will, of steroids. By just convention, I think, I think that they used Decadron as a factor of a hundred, and then compared every other steroid to your Decadron's potency, the natural steroid, by the way, hydrocortisone would be about 25. So it's about four times more potent than the natural steroid.**

So triamcinolone, as you can see on this table, is two or three times more potent than is Decadron. But the other steroids we talked about today, including fluticasone, Flonase, is 18 times more potent.

This, by the way, is a receptor binding assay. This is not the MacKenzie Skin Blanching assay. The numbers are close to this, but not quite the same on the MacKenzie

assay.

Q. **Are there any other potency-related factors that would determine the usefulness of a corticosteroid?**

A. **There are a lot of ways steroids work. And so they -- what happens is the steroid has to get into the cell and bind to its receptor, which activates the process.**

The longer it binds to its receptor, the more it stimulates it.

So here is the binding half-lives. You can see that most of the steroids are relatively similar one to the other, but that fluticasone, Flonase, is substantially more firmly bound to the receptor.

Q. **Do you know the relative dosing of Flonase and Nasacort AQ?**

A. **It is, to me, a surprise that triamcinolone acetonide is equally potent to Flonase, fluticasone, as a nasal spray. I have always found that surprising. But it is surprising that even though everything would say Flonase should be seven, eight times better, it is not. They are equally potent.**

Q. **You said they were equally opponent. Is there other evidence of efficacy in the body, in the nose, that leads you to that conclusion?**

A. **Well, there have been a number of studies. This is one of a number of studies that looks at symptom scores.**

What you can see is, in the capability of both Flonase and Nasacort, triamcinolone acetonide and fluticasone, to reduce symptoms, they are both identical. Despite the fact one is much more potent than the other. On a microgram per microgram basis, they are equal efficacy.

Q. **Is there any difference between the two in terms of their ability to affect the inhalation process?**

A. **In terms of congestion, this is a study that was done by Eli Meltzer here. He is looking at peak, nasal respiratory primary flows. Once again, it's another demonstration. But that first one was symptoms scores. This is an objective measurement of nasal air flow. You can see again that triamcinolone is just as good or in this case better than fluticasone, surprisingly.**

Q. **Are you certain in the two Phase 3 clinical trials whether there was a CRO involved or whether Rhone-Poulenc Rorer maintained direct control over these tests?**

A. **You know, I was not a study participant in either of the trials. So I really can't answer that question. Usually, a CRO is involved.**

Q. **But you don't have a clear recollection?**

A. **I was not in the trial.**

Q. **But you did review the material --**

A. **I reviewed all the protocols.**

Q. **Approximately how many boxes of materials did you**

review in that process?

A. Well, you mean -- I have received a cubic meter of paper from you, which I have looked at. It's occupying a lot of my study.

Q. I apologize, both to you an the environment again.

I would like to change the topic quickly to some of the testimony that we heard yesterday. And you heard Dr. Donovan talking about, she stood up here and she made a drawing, and I know she focuses mainly on pharmaceutical formulations, what's in the bottle, not the bottle or the pump, but she stated in her testimony that Nasacort AQ might get trapped in the nasal valve, might not make it beyond that point as any sort of plume, any sort of mist. Is that consistent with your experience?

A. No. We instruct -- I did it yesterday. We instruct patients to put the nozzle of the spray inside the vestibule, so it's past the entrance to the nasal valve and sprayed up toward the eye and slightly laterally, which is where the largest space is in the nose. I use these sprays, somebody mentioned about their wife, I use these sprays personally. I test all the sprays myself. I have hay fever, and I use these sprays every single day. And you can feel the spray on top of your nose. It sprays throughout the nose.

Q. Dr. Donovan also testified, as you heard in the

discussion between the lawyers and the Judge, that in all her years of experience in their area of study, she had never heard of a nasal spray that reliably reached any of the sinuses, much less the frontal sinus. Is that consistent with your knowledge of treatments for sinus disease, including frontal disease?

A. **Well, a spray is an atomized dispersion of a liquid into air that is sprayed into the nose. And these sprays are a hundred microliters apiece. A hundred microliters is the volume. A thousand microliters is a milliliter. And there would be five milliliters in a teaspoonful.**

So a hundred microliters is a small amount of spray. And that's why, I mean, you would not consider using these products or studying these products for sinusitis. The sinuses require a different approach.

So what's been done recently has been to nebulize products into the nose. So a nebulization is what -- you take a milliliter or two, so half a teaspoonful, and you oscillate it or spin it, and break it up into fine particles and it's put in a prong in the nose and you breathe it. You are just breathing an aerosol of a spray. But instead of a hundred microliters you are breathing in two milliliters. And instead of using triamcinolone they are using mometasone which is another steroid, it is Nasonex. And that's what's being done with thousands of

patients today for the treatment of sinusitis. And it is being used because these nebulized products get into the sinuses.

When I heard her say that no product is on the market today so that you could breathe in for the sinuses, that is just absolutely wrong.

Q. You said that it was an aerosol. By saying that did you mean that this was a CFC or HFA-propelled product?

A. Well, I mean, the nasal aqueous spray is an aerosol. You are making a dispersion of small particles, usually between 5 and 20 microns. And that's exactly what you do with the nebulizer. You have reduced this nebulized product, which is a milliliter or two versus a hundred microliters, it is the same exact process of breathing. You are breathing it in. And because breathing communicates, ventilates the sinuses, it gets into the sinuses and in many cases it treats the sinusitis.

Q. Now, you are saying treating sinusitis. Do you have to treat sinusitis to treat rhinitis?

A. No, no, no. I mean, they are very different diseases. I think Eli said, rhinitis is inflammation of the nose and sinusitis is inflammation of the sinuses. You may recall, there are sinuses around the eyes, the frontal sinus is the one, of course, everyone is focused on here, and that is above the eyes and somewhat between the eyes as well.

So they are a very different disease. They are a much different disease.

You often have rhinitis as a cause for sinusitis, but you certainly have sinusitis without rhinitis.

Q. I would like to put up what has probably been the most common slide in this trial. I just wanted to get an idea, it says the lateral wall of the nose without turbinates.

A. Right.

Q. Does that give you the complete picture of the size and shape of the frontal sinus?

A. Well, yes. In the plane that this picture is taken, it is a lovely depiction. What it looks like is the frontal sinuses an inch or two above the opening into the frontal sinus.

But, remember, this is a plane. This is a picture of a certain cut.

Could I draw? I am not a good artist but...

THE COURT: That's fine.

(Witness steps down from stand.)

A. First of all, you have to understand that frontal sinuses are by far the most variable sinuses. So many of us, some people in this room have no frontal sinuses. Those sinuses, even though they are variable, usually have an indentation like that, let me put this in perspective, so

the eyebrow and the eye would be here and the nose here. And there is a dip into the center.

What that plane was, was taking a picture right here, whereas if you had taken a picture here, it would have dipped much further down into the nose.

Here is the eyeball. And this is the frontal sinus. And in the picture that we have all been using is a cut right here. And if you took a cut about a quarter of an inch over, it would dip much further down.

So if you looked at the side picture of the nose, the frontal sinus would come down a little bit toward the ethmoid sinuses which they share a wall with.

So it's much closer to the area where the sinus drains than it looked like in that particular picture that all of us have been using.

I found an x-ray.

(Witness resumes stand.)

This is an x-ray. These x-rays are actually quite simple to understand, I think.

What you are looking at here is the inferior turbinate. This is the maxillary sinus, the big sinus in your cheeks. This is the middle turbinate, here and here. And this would be the dip-down that I was talking about of the frontal sinus. And this is the sinus outthrow tract right here.

It is not anywhere near as complex as the drawings made it look like. Actually, it's just right here, you are breathing in. Air is going around this middle meatus. All it has to do is go right there. That is the entrance.

I don't know, it's pretty straightforward to me.

So I have no problem at all perceiving of air going in here. And I know the nebulized treatment I use for my patients gets into the sinuses. And I know when I fly in airplanes I never have a problem with my frontal sinuses, but I have problems with my ears. So I am pretty confident that this open space communicates with the air.

Q. **Now, Dr. MacKay testified he is familiar with nasal anatomy from being an ear, nose and throat surgeon and having visualized the inside of a nose many times. Have you ever looked inside the nose?**

A. **Well, I am one of the allergists who do rhinoscopy every single day. So I am into people's noses as much as I possibly can be. But I am not a surgeon, and I have never dissected the frontal sinus. We did have an interesting dissection of one, which I would like to get back to if we could.**

This is a very complicated drawing. I know everybody in this room is looking at this saying what in the heck is this.

I am not -- I never saw this until yesterday.

But what you are looking at here are a honeycomb of ethmoid air cells. There are four of them on either side of the nose. Dr. MacKay pointed out this very torturous track. I think it's called the semi-linear hiatus into which the frontal sinus drains right down here, then there is a stream that goes back down your throat.

This particular dissection is interesting in that this patient has a few abnormalities. One is he has two openings into the maxillary sinuses, which we see three or four or five percent of the time but not very frequently. And this tract, this is a recess. This is not a duct. It's not closed. This is an open recess. What you are missing, this cut right here is the middle turbinate that has been dissected away. But there is no closure on this. This is an open roof. And this is the front of your nose.

If your finger was long enough, you would reach this spot with your little finger if you put it in. This is where the vestibule is down here. You are not very far from -- when we spray a spray, we direct patients right at this spot.

Well, this looks kind of torturous right here, and that's because this particular section has an extra air cell in it.

This cell, it's got a bunch of -- you see it in

about 20 percent of people, and it predisposes towards sinusitis. But this is an abnormality, as is the extra maxillary ostea. This space which looks tight and closed is artificially closed because this is an abnormal patient. This patient has an extra air cell here that you and I don't have. So this is a peculiar demonstration. Here is the frontal sinus, though. And here is this recess.

That's where the product has to go. Ordinarily, that is an open space. And as I showed on the last picture, that's widely open.

Now, the outflow goes this way. But breathing would go this way. And that's nothing. I don't see left-hand turns and loop de loops. I see a direct spray going to this area quite readily, especially the way we direct nasal sprays in our patients.

Q. What do you mean especially the way we direct nasal sprays?

A. You tell patients to aim up at the inner corner of the eye and sniff in. The sniff, as I said yesterday, if you all sniff (indicating), it goes right to the top of the your nose, which is directly where this is.

Q. Now, let me get this straight. Let me see if I understand. Does the inflow, the way into the frontal sinus have to go through this long tube-looking feature?

A. I don't think so. Why would it? I mean air flows

under the middle turbinate and would be right here and go down. This is close because of this bone here, this extra air cell, but it would go right there. That is all it has to go.

Q. So it's like an indoor and an outdoor?

A. The outflow tract is absolutely down the semilunar hiatus and it goes here. And there is a well prescribed exit flow that you can see in patients when they have perennial drainage. But the inflow is just right here.

MR. RICH: Thank you, Dr. Kaliner.

Your Honor, I have no further questions.

THE COURT: Counsel, you may cross-examine.

CROSS-EXAMINATION

BY MR. GRACEY:

Q. Hi, Dr. Kaliner, again. It always seems when you have a flight to catch, I'm in your way, Just like from your deposition the last time. But let me try to be brief so you can try and catch your plane.

Just kind of picking up on where Aventis's counsel left off. Are you saying that the frontal ethmoidal recess is the frontal sinus?

A. No.

Q. Okay. And just so we're clear for the Court, Dr. MacKay operated on the frontal sinus, I think it was thousands of times; right?

A. **I think he said a thousand.**
Q. **Okay. And you have never operated on the frontal sinus, yourself. Right?**
A. **No, I haven't.**
Q. **Okay. And, in fact, as far as the nasal anatomy goes, you would agree with me that Dr. MacKay has far more experience in the nasal anatomy due to his operating on the nasal anatomy. Isn't that true?**
A. **Well, I wouldn't agree with that, no. I mean I take care of patients. I probably have seen, in terms of doing nasal examinations, I bet I've seen more patients than anyone in this room, including Dr. MacKay. I mean I'm a very careful examiner.**
Q. **And I believe you are. But when you do your examinations, you don't look into the frontal sinus, do you?**
A. **No. You can see the anterior aspect of the middle turbinate in nearly every patient. And I, because so many patients come to me because of difficult to manage sinus disease, it's an area of prime interest for me. I look carefully at every patient; and I do a number of rhinoscopies which pulls me right to that space.**
Q. **Dr. Kaliner, I wanted to talk to you just for one minute.**
MR. GRACEY: If we could pull up -- actually, since it was one of your demonstratives, I'll use the Elmo.

I'll have to take your pretty picture away.

THE COMPUTER TECHNICIAN: I have the image.

MR. GRACEY: Oh, you have the image? Great.

BY MR. GRACEY:

Q. **I believe it's the same image you were looking at.**

A. **Right.**

Q. **I think you testified that this here and here was the frontal sinus. Was that what you said?**

A. **It's the bottom part. It's the most central part of the frontal sinus.**

Q. **Okay. Let's be clear about a couple things. First, this is a CT scan. Right?**

A. **This is a CT scan.**

Q. **It's not an actual picture like we were looking at, that you were looking at?**

A. **A dissection.**

Q. **Correct.**

A. **No, it's not a dissection.**

Q. **Isn't it true, doctor, that this is the ethmoidal sinuses right here?**

A. **The ethmoid sinuses are here. This is the frontal.**

Q. **Okay. Dr. Kaliner, you had testified a little bit about public use, and I wanted to ask you some questions about that.**

MR. GRACEY: You can take that down.

BY MR. GRACEY:

Q. You're aware that the Kobayashi study occurred, started about December 1992? It was the 305 study.

A. I'm going to take the word for you. The answer is I don't know that.

Q. And it continued until about March '93.

A. Okay.

Q. About three or four months later. There was 178 patients enrolled in that study. Right?

A. Yes.

Q. Now, I think you testified that the patients knew the drug that they were taking. Right?

A. They knew the active ingredient, right.

Q. In fact, they knew they were taking an aqueous version of Nasacort, didn't they?

A. They knew it was a triamcinolone aqueous spray and there was an analogous product on the market.

Q. In fact, that analogous product was identified for them as Nasacort, wasn't it?

A. (Nodding yes.)

Q. Okay. Now, none of the investigators were employees of RPR, were they?

A. No.

Q. And Dr. Kim, the inventor of the patents at issue, was not an investigator, was he?

A. **No, he was not.**
Q. **Indeed, Dr. Kim, the inventor, did not run these studies, did he?**
A. **I don't think he had anything to do with them.**
Q. **Right. He didn't have anything to do with them. He didn't control them either, did he?**
A. **No.**
Q. **Now, these studies were conducted at -- I'm speaking specifically with regard to the 305 study, which is the DX-158 for the record. These studies were conducted by six investigators from six independent centers from RPR. Isn't that right?**
A. **Yes, that is correct.**
Q. **Now, the patients, they weren't required to stay at the study centers, were they?**
A. **No, no.**
Q. **And there are study centers that are set on campuses, aren't there?**
A. **For Phase I and Phase II trials, there are. But in allergy, no.**
Q. **These patients didn't have to take the Nasacort AQ there at the center. Right? They left the center and took it wherever they wanted. Isn't that right?**
A. **Yes. The way we do it, usually we start off the patients on the first day showing them how to use the**

products in the office; but then they're on their own, having been trained, and they take it on schedule at home.

Q. No restrictions about where they could take it. They weren't told to go hide in a closet, take your Nasacort and come back out?

A. They're told to take it the same time every day.

Q. And that could be anywhere. It could be in their home? Could be their office?

A. (Nodding head yes.)

Q. Is that is a yes?

A. Yes, that's correct.

Q. It could be in their car? It could be at a Phillies game?

A. There is no restrictions.

Q. None whatsoever. Right.

Now, you testified you didn't think the educational level of the people that were participants in the study was particularly high. That is what you'd said.

A. I said, by and large, the people who volunteer for studies are not the most well educated people that we have.

Q. But you're not claiming to have looked into the educational background of every single volunteer that took part in the study. Right?

A. No, I have interacted with thousands of volunteers but I was not a study site for this particular study.

Q. **In fact, any of these participants could have been a chemist or married to a chemist. Right?**

A. **(Nodding head yes.)**

Q. **You are nodding your head.**

A. **The answer is yes, they could have been. It could have been anybody.**

Q. **They could have been a formulator?**

A. **That's correct.**

Q. **They could have been married to a formulator?**

A. **They could have been.**

Q. **They could have taken this at work?**

A. **They could have.**

Q. **And their coworkers could have been formulators?**

A. **They could have.**

Q. **They could have been Ph.D.s?**

A. **You can take this dream anyplace you want to.**

Q. **Okay. Thank you. In the interest of getting on your flight, that is far enough for me.**

Now, I think you stated, but I just want to make sure the record is clear, these participants were under absolutely no obligation of secrecy. Isn't that right?

A. **I mean they knew what they were -- they knew the active ingredient and they were not restricted. Matter of fact, they have to know that, by law, to know what they're taking.**

Q. **I appreciate that. I was asking a slightly different question but I appreciate that answer. My question actually was these volunteers, these participants taking the Nasacort AQ were under absolutely no obligation of secrecy?**

A. **Right. They were not.**

Q. **Right. They could tell the world that they were taking Nasacort AQ?**

A. **Correct.**

Q. **They didn't sign any confidentiality agreement, did they?**

A. **They signed an informed consent.**

Q. **They signed an informed consent. And that actually told them they were taking triamcinolone acetonide. Right?**

A. **Right.**

Q. **They told them it was an aqueous form of triamcinolone acetonide?**

A. **Right. That's the experiment. Correct.**

Q. **Now, just quickly, there was also the 309 study, which is DX-155 for the record. And in that study, I believe there was about 429 patients that took part in that study. Does that sound right to you?**

A. **Sounds about right.**

Q. **All right. And that study started in August of 1993 and ended in about October of 1993. Does that sound right?**

A. **That sounds about right.**

Q. **All right. So in that study, there was likewise no restrictions on where the participants could take the drug. Right?**

A. **Yes, that's correct.**

Q. **And there was likewise no obligation that they keep their use of Nasacort AQ secret. Right?**

A. **That's correct.**

Q. **And I won't ask you the questions but it could have been anybody that was involved in that study. Right?**

A. **That's correct.**

Q. **All right. So combined between the 305 study and the 309 study, you had about 600 participants taking Nasacort AQ. Correct?**

A. **That's correct.**

Q. **All right. Now, you had testified that Dr. Donovan referred to nasal sprays. Actually, I don't know that you testified. I think plaintiffs' counsel represented what Dr. Donovan stated, but --**

A. **Right.**

Q. **-- you recall the questions and answers. Right?**

A. **Yes, I do.**

Q. **All right. And there is actually a difference between a nasal spray and a nebulizer, isn't there?**

A. **Yes, there is a difference. Right, there is a difference.**

Q. **Okay. A nebulizer is something that you actually breath into your nose for several minutes. Isn't that right?**

A. **That's correct. That's the big difference.**

Q. **Right. And a nasal spray, it's just one puff?**

A. **One or two puffs. That's correct.**

Q. **Okay. Now, you know, don't you, based on your experience that you have on the use of nebulizers, that a nebulizer can create an ultrafine mist of particles as much as 50 times smaller than a nasal spray such as Nasacort AQ. Isn't that right?**

A. **These are not ultrasonic nebulizations. There are ultrasonic nebulizers, but the products that we're talking about here, dispensing mometasone in a nasal nebulizer uses a device that puts out a 5-to-15-or-20 micron particle.**

Q. **Smaller than the nasal spray such as Nasacort AQ. Right?**

A. **Nasacort is 5-to-15, 5-to-20 microns.**

Q. **Dr. Kaliner, I want to jump gears a little bit somewhat related those to the two studies we were talking about. You believe that if you demonstrate that a nasal spray is safe and effective -- okay? -- safe and effective for the treatment of perennial allergic rhinitis, you would anticipate that the same product would work to treat seasonal allergic rhinitis. Isn't that right?**

A. **You would anticipate.**

MR. GRACEY: You're going to make your flight. Thank you so much for coming in.

THE COURT: Thank you, counsel.

Redirect.

MR. RICH: Very short, Your Honor. Thank you very much.

REDIRECT EXAMINATION

BY MR. RICH:

Q. **Now, he just asked about whether you would anticipate if something worked for seasonal allergic rhinitis, if it would work for perennial allergic rhinitis. Would the FDA accept something for perennial allergic rhinitis if you had shown that it was effective for seasonal allergic rhinitis?**

A. **Absolutely not. They require well-controlled, placebo-controlled trials to demonstrate effectiveness in PAR, just like they do in SM. So there is no extension.**

Q. **And there was some questions about these specific trials whether someone was taking Nasacort AQ. In the materials that you read, was anything described as Nasacort AQ?**

A. **I don't think so. I think it was called, it was triamcinolone acetonide.**

Q. **And just very quickly, if I could bring the x-ray up, I was reminded that I had you point places and not describe**

where they were.
A. Right.
Q. If you could tell me where on this picture, in words, the frontal sinuses are?
A. So as I outline the space here, this is the ethmoid, anterior ethmoid air cell. And this is the most deepest penetration of the frontal sinus into the nose. And it's inside the middle turbinate above the ethmoid air cell and lateral to the eyeball, which would be right here.
This space, what is called the ostiomeatal complex, this opening that is below this ethmoid air sell is the entrance to the maxillary sinus. So you can see how close things are when you dissect them apart by x-ray.
Q. So looking to the right side of this CT scan, the top dark space is the frontal sinus?
A. It's the lowest part of the frontal sinus.
Q. Just below that, there is an enclosed dark space. That is the ethmoidal sinus?
A. Yes, that air cell right there.
Q. And at the bottom right, there is a dark space. That is the maxillary sinus?
A. That is correct.
Q. Among the lighter areas on the figure, there is kind of a fishhook shape.
A. So the light areas actually are bones. This is the

middle turbinate. This is the middle meatus space between the turbinate and the entrance to the frontal sinus, maxillary sinus and ethmoid. This is the inferior turbinate. This is the nasal septum.

So you seeing the nasal septum in the middle. And the two lateral bones, or these compo bones, this happens to be inverted shape, they're usually bent the other way. Nevertheless, that's the way this one is. And they outline the entrances to the sinuses. And the air space, when you breathe through the back of the nose, is the space between the turbinates and the septum that I'm outlining right now.

Q. So just describing, trying to describe them in words, the J-shaped, fishhook-shaped feature, light feature from the top going down to the bottom, is the middle turbinate?

A. Middle turbinate at the top part of the nose and inferior turbinate at the bottom half of the nose.

MR. RICH: And if we could look at the other feature the histological slide.

MR. GRACEY: I'll just object. It's beyond the scope, Your Honor.

THE COURT: I'm sorry?

MR. GRACEY: Object. Beyond the scope of my cross.

MR. RICH: I'm just trying --

MR. GRACEY: He is just repeating.

MR. RICH: All I'm trying to do is describe what he said with the laser pointer in words.

THE COURT: Go ahead.

BY MR. RICH:

Q. At the top left, there is an opening. And that is the frontal?

A. This would be the frontal sinus at the top left part of the screen. This is analogous parts of the frontal sinus that is coming down the most deepest part of the frontal sinus.

This is the ostia.

This space at the top part of the picture that is quite narrowed in this particular dissection is the opening into the frontal sinus.

THE COURT: You don't recall him testifying about this?

MR. RICH: Your Honor, I wasn't trying to have him testify.

THE COURT: I mean he described it just the way he is doing it now. I think the record is clear.

MR. RICH: Okay. Thank you, Your Honor. Then I have nothing further.

I appreciate Your Honor's indulgence.

And thank you very much to the court reporters

for their time.

THE COURT: All right. Thank you, doctor. You may go to your flight.

THE WITNESS: Thank you.

THE COURT: Counsel, how many more witness does you have on rebuttal?

MR. BERGHOFF: I want to confer with colleagues. I think we will be trimming down our list. And I will confidently represent -- and I rarely do this -- that we will be finishing early tomorrow. We will not be going until 4:30 or 5:00.

THE COURT: Oh, I didn't anticipate we would.

MR. BERGHOFF: I was hoping that was correct; and that is going to be the fact.

THE COURT: Yes, I'm just trying to get a handle on how many, roughly, ballpark.

MR. BERGHOFF: Three or four witnesses. And we don't have any that are going to be extended marathons.

THE COURT: You can sit down.

MR. BERGHOFF: Thank you, Your Honor.

THE COURT: I'll preview something for both sides that I'm contemplating doing. And that is I'm considering having the parties simultaneously submit proposed findings and conclusions by May 30th of no greater length than 15 pages a piece. I'll leave myself some wiggle

room on this, but it seems to me that this case is coming down to the fact finder's impressions largely of expert testimony. And, ultimately, this is going to be determined as much as a matter of fact in this case as a matter of law. And I would rather visit that issue or those issues while things are relatively fresh in my mind; just as a jury would have the opportunity to immediately upon receiving instructions and hearing your closing speeches on that subject.

I may or may not entertain closings on June the 9th, which is when we're going to meet. I'm thinking about having you back at 9:00 o'clock. I'll be on a patent trial at that time so my time is going to be short.

MR. DAY: I'll be with you.

THE COURT: You're involved, yes.

So that is what I'm thinking about. You can prepare your minds. I'm pretty sure that that is the course I'm going to take.

If, over the course of the evening, in thinking about what I'm saying, you determine that or you think that you can demonstrate good cause as to why I should give you more than 15 pages, I'll give you a chance to convince me, but it seems to me that 15 pages should be enough. Okay?

All right. Counsel, see you in the morning.

(Trial adjourned at 4:55 p.m.)